ABN abstracts

Association of British Neurologists Spring Meeting, Brighton, UK, 19–21 April 2006

Platforms

001 CLINICAL FEATURES AT DISEASE ONSET IN 1000 PATIENTS WITH MULTIPLE SCLEROSIS

C. L. Hirst, T. P. Pickersgill, N. P. Robertson. *Department of Neurology, University Hospital of Wales, Cardiff, Wales*

Phenotypic variability contributes to difficulties developing patient specific interventions. Analysis of clinical features in early phase disease may allow prediction of disease severity and inform therapeutic decisions for clinicians and patients prior to onset of axonal degeneration.

A prospective clinic based cohort of 1000 patients seen over a 20 year period were identified. All patients met clinical criteria for multiple sclerosis and serial follow up data was available. Sex ratio 1M:2.4F, mean age at onset 31.6 years and mean age at diagnosis was 36.5 years. At presentation 78.8% patients recovered fully from initial relapse, 2.1% had progressive disease, 60.2% patients had symptoms of long tract involvement, 20.5% brainstem, 19.3% cerebellar and 10% optic nerve. Isolated optic neuritis occurred in only 3.2% patients. 174 patients presented with involvement of multiple anatomical sites. Mean time from onset to progression in 20% of patients was 10.65 years. The proportion of patients reaching EDSS 6.0 rose from 17% in those patients with disease duration of 0–5 years to 48% in the 15–20 year group.

These data suggest that primary progressive disease is an unusual presentation and that the therapeutic window for interventions targeted at the inflammatory component of disease closes for 20% of patients within 4 years of diagnosis, and 50% have developed a severe level of irreversible disability 15–20 years after disease onset.

002 THE CLINICAL CHARACTERISTICS AND TREATMENT OF IDIOPATHIC CENTRAL NERVOUS SYSTEM HYPERSOMNOLENCE

K. N. Anderson, I. E. Smith, J. M. Shneerson. *Respiratory Support and Sleep Centre, Cambridge, UK*

Idiopathic central nervous system (CNS) hypersomnia is defined as a cause of excessive sleepiness consisting of prolonged sleep episodes of non-rapid eye movement sleep. In comparison with narcolepsy, the clinical, polysomnographic, and immunogenetic features are poorly characterised and surprisingly little is known about the clinical course and response to treatment.

Within Papworth Hospital, 101 patients had a diagnosis of Idiopathic CNS hypersomnia made over an 8-year period. All had sleep scores, polysomnography and HLA typing and the clinical characteristics and management of these patients is presented here.

Patients were followed up for a mean of 38 months and tended to present in the third decade but had often had symptoms for many years. The majority had prolonged slow wave sleep and all were negative for the HLA DR15 haplotype seen in Narcolepsy. 69 patients were treated with Modafinil.

Two main groups emerged; one third had a more benign phenotype with a shorter history of symptoms, a more rapid and sustained response to stimulants such as Modafinil, and occasionally spontaneous remission. A second group had higher sleep scores, longer history and often required much higher doses of stimulants. This represents the largest UK series of patients with this condition.

003 THE SEIZURE OUTCOME AFTER AMYGDALAHIPPOCAMPECTOMY AND TEMPORAL LOBECTOMY

U. C. Wieshmann, H. Bate, P. Eldridge, T. Varma. *The Walton Centre for Neurology and Neurosurgery, Liverpool, UK; University of Bristol, Bristol, UK*

Aims: The aim of this study was to compare the seizure outcome of two different types of epilepsy surgery, selective amydalohippocampectomy (AHE) and anterior temporal lobectomy (ATLE) in patients with temporal lobe epilepsy.
Methods: 114 patients with non lesional temporal lobe epilepsy were included. Patients had ATLE if the non dominant hemisphere was affected or if the whole temporal lobe was atrophic. Patients had AHE if the dominant hemisphere was affected. Standardised seizure outcome at 1 year following surgery was used.
Results: Overall 40% of the 114 patients who had temporal lobe epilepsy surgery were seizure free at 1-year (Engel's class Ia). A good outcome (Engel's classes I and II) was significantly more frequent in ATLE than in AHE. (66% and 44% respectively, $p = 0.03$)
Conclusions: ATLE had a better seizure outcome than AHE.

004 TEN YEARS EXPERIENCE OF A DRUG REACTION PROTOCOL IN THE PRE-SURGICAL ASSESSMENT OF PATIENTS WITH FOCAL EPILEPSIES

T. Foltynie, C. Scott, P. Korlipara, S. J. Smith, M. C. Walker. *National Hospital for Neurology & Neurosurgery, Queen Square, London, UK*

There is little published data on the safety and effectiveness of drug reduction in the pre-surgical assessment of focal epilepsies. During a 10-year period (1/1/95–1/1/05), the Telemetry Unit at Queen Square, London, UK, performed a total of 1228 scalp EEG recordings on a total of 928 new pre-surgical patients. A simple protocol of anti-epileptic drug reduction has been in place over this period. 551 patients met guidelines for drug reduction—77% had seizures with 14% becoming generalised. 377 patients were considered unsafe for drug reduction—58% had seizures, 9% generalised. Patients with frontal seizures were more likely to become generalised. 2 patients could not be discharged following their telemetry due to seizure complications (drowsiness/psychosis). No deaths occurred.

Of the 709 patients only requiring 1 visit, 302 were appropriate for surgery, with 149 keen to proceed at discharge. Up to 5 admissions were required for some patients to ultimately conclude with referral for surgery. 1 patient died while waiting for intracranial EEG having had no seizures during scalp recording when not drug reduced, and non-localisable generalised seizures following drug reduction. No other adverse events occurred among patients waiting for repeat telemetry. Our drug reduction policy appears effective while remaining sufficiently safe.

005 ETHNIC DIFFERENCES IN STROKE RISK FACTORS AND STROKE SUBTYPE – FIRST RESULTS FROM THE SOUTH LONDON ETHNICITY AND STROKE STUDY

U. Khan, P. Jerrard-Dunne, J. Birns, I. Burger, A. Evans, R. McGovern, L. Porteous, A. Rudd, C. Wolfe, H. Markus. *Clinical Neurosciences, St George's University of London, London, UK; Departments of Public Health Sciences and Stroke Medicine, Guy's, King's, and St Thomas' School of Medicine, London, UK*

Introduction: The South London black population has a two-fold increase in stroke incidence compared to whites. This increase may be due to stroke risk factor and subtype differences in blacks. Our study investigates the causes of this increased incidence.
Methods: Consecutive, prospective recruitment of black and white strokes was performed. All cases underwent standardised clinical assessment, data collection and stroke subtyping by one individual.
Results: Black stroke cases had increased hypertension (OR 2.83 (1.91 to 4.20) $p<0.001$) and diabetes (OR 2.60 (1.81 to 3.74) $p<0.001$) and

were younger (OR 0.96 (0.95 to 0.98) p<0.001), had less smoking (OR 0.33 (0.23 to 0.47) p<0.001), atrial fibrillation (OR 0.27 (0.18 to 0.42) p<0.001) and myocardial infarction (OR 0.55 (0.31 to 0.98) p<0.041) compared to whites. The black stroke cohort had increased small vessel disease (SVD) (OR 3.05 (2.26 to 4.11) p<0.001) but less large vessel atherosclerotic disease (OR 0.46 (0.31 to 0.68) p<0.001) and cardio-embolic disease (OR 0.55 (0.41 to 0.73) p<0.001) compared to whites. African-Caribbean strokes were older (OR 1.07 (1.05 to 1.09) p<0.001) with increased male sex (OR 2.75 (1.65 to 4.57) p<0.001) and smoking (OR 6.98 (4.01 to 12.13) p<0.001) compared to Africans. The African stroke cohort had increased primary intracerebral haemorrhage (PICH) (OR 1.98 (1.17 to 3.34) p = 0.010) compared to African-Caribbeans.
Conclusions: Increased hypertension, diabetes and SVD may contribute to the increased incidence of stroke in blacks. Africans are younger and have increased PICH compared to African-Caribbeans.

006 MAGNETIC RESONANCE SPECTROSCOPY AND COGNITIVE FUNCTION IN CEREBRAL SMALL VESSEL DISEASE

A. Nitkunan, R. A. Charlton, T. Barrick, D. J. O. McIntyre, F. Howe, H. S. Markus. *Centre for Clinical Neuroscience and Dept of Basic Medical Sciences, St George's, University of London, Cranmer Terrace, London*

Introduction: Cerebral small vessel disease (SVD) is an important cause of cognitive impairment and dementia but the pathophysiological mechanisms remains unclear. We characterized brain metabolic differences between SVD patients and controls using magnetic resonance spectroscopy and correlated this with neuropsychology.
Methods: 35 patients with SVD (lacunar stroke and radiological leukoaraiosis) and 35 controls underwent neuropsychology tests and multivoxel chemical shift imaging (CSI) of the white matter. Differences in the metabolite ratios for N-acetylaspartate (NAA, a neuronal marker), creatine (Cr) and choline (Cho) were determined. Cognition was correlated with CSI in patients. A subset of 20 subjects underwent single voxel imaging to obtain absolute metabolite concentrations.
Results: Single voxel analysis revealed reductions in NAA, choline and creatine by 16.59% (p = 0.0003), 20.43% (p = 0.0004) and 14.98% (p = 0.001), respectively. CSI analyses revealed significant reductions in NAA/Cr and NAA/Cho ratios in patients compared to controls (lower by 9.14% ($p = 6\times10-5$) and 6.64% (p = 0.021) respectively). Neuropsychology did not correlate with CSI metabolite ratios.
Conclusion: The global reduction in the absolute metabolite concentrations suggests widespread white matter tissue damage. The lack of correlation with cognition does not support the use of MRS as a surrogate disease marker.

007 POPULATION CHARACTERISTICS MAY CONTRIBUTE TO THE SUCCESS OR FAILURE OF DISEASE MODIFYING THERAPY IN MULTIPLE SCLEROSIS

B. Wakerley, A. Jacob, J. Ramtahal, S. Rashid, B. Polito, J. Chataway, C. Young, M. Boggild, O. Malik, R. Nicholas. *Department of Cellular & Molecular Neuroscience, Imperial College, Charing Cross Hospital, London, UK; Department of Neurosciences, University of Liverpool, Walton Centre for Neurology and Neurosurgery, Liverpool, UK; Department of Neurology, St Mary's Hospital, London, UK*

Background: With the advent of DMTs and the perceived requirement for long-term therapy in multiple sclerosis, it is essential to identify the reasons for treatment failure.
Aim: To identify reasons for first line DMT failure in two UK prescribing centres.
Methods: DMTs were prescribed according to Association of British Neurologists guidelines. Treatment failure was defined as stopping treatment due to continued disease activity/perceived non-benefit or side effects.
Results: We studied 190 subjects from Liverpool and 155 from London. Prior to therapy annualised relapse rates (ARR, mean $\pm$ SE) were increased in Liverpool (1.37 ± 0.03) compared to London (1.19 ± 0.06, p<0.0001) while there was no difference in disability scores. Treatment failed in 91 (48%) subjects from Liverpool and 40 (26%) from London (p<0.0001), continuing disease activity accounting for 60 (66%) from Liverpool and 23 (58%) from London. In Liverpool the ARR was 0.35 ± 0.09 in subjects who continued DMTs, 0.44 ± 0.15 in treatment failures due to side effects and 1.52 ± 0.25 in treatment failures due to continued disease activity (p<0.0001) whereas in London no difference in ARR was seen between the three groups.
Conclusions: The failure rate of first line therapy is significantly different in two geographically separated centres. This may reflect differences in the population treated.

008 MAKING SENSE OF MAGNETIC RESONANCE MEASURES IN MULTIPLE SCLEROSIS: THE POST MORTEM EVIDENCE

K. Schmierer, D. H. Miller. *NMR Research Unit, Institute of Neurology, University College London, London, UK*

Magnetic resonance is being used to monitor multiple sclerosis. Conventional magnetic resonance images (cMRI) display multiple sclerosis white matter lesions (WML) with high sensitivity. However, cMRI indices correlate poorly with disability, in part due to lack of pathological specificity. Quantitative magnetic resonance (qMR), including magnetisation transfer (MT), relaxation time (RT), diffusion, and magnetic resonance spectroscopic (MRS) metabolite measures may be more specific. We have performed magnetic resonance in 36 fresh samples of post mortem (PM) brain to enable direct correlation of magnetic resonance with pathology. These studies have produced insights into underlying pathology of four magnetic resonance modalities: (i) In WML the degree of hypo-intensity on T1W MRI correlates with myelin content and axonal count. (ii) MT ratio (MTR) correlates primarily with myelin content and secondarily with axonal count. (iii) T1-RT correlates with myelin content, however secondarily to correlation between MTR and myelin. (iv) Mean diffusivity and fractional anisotropy are associated with myelin content and axons and – less so – gliosis. Future studies will investigate additional indices of MT and MRS metabolites. High-field magnetic resonance may in the future (i) improve co-registration between magnetic resonance and histology and (ii) facilitate the characterisation of grey matter pathology.

009 SPINAL CORD GREY MATTER IS A PREDILECTION SITE FOR DEMYELINATION IN MULTIPLE SCLEROSIS

Gilmore. CP, Bö. L, Owens. T, Lowe. J, Esiri. M, Evangelou. N. *Queens Medical Centre, Nottingham; VU Medical centre, Amsterdam, The Netherlands; Department of Economics, University of Nottingham, Nottingham, UK; Department of Neuropathology, University of Nottingham, Nottingham, UK; Department of Neuropathology, Oxford Radcliffe NHS Trust, Oxford, UK*

Objective: To assess the extent and pattern of grey matter (GM) demyelination in the spinal cord in multiple sclerosis.
Methods: Autopsy material was obtained from 36 multiple sclerosis cases and 12 controls. Transverse sections were taken from 5 levels of the spinal cord and the extent of GM and white matter (WM) demyelination evaluated using proteolipid protein (PLP) immunohistochemistry.
Results: In comparison to conventional staining techniques, PLP-staining was more sensitive at detecting GM demyelination. The proportion of the GM that was demyelinated (33%) was significantly greater than the proportion of demyelinated WM (20%) (p<0.0001). Similarly, demyelination was more extensive in the GM than in the WM at each of the 5 cord levels.

The extent of GM demyelination was not significantly different between the 5 cord levels.

Morphologically, the borders of a proportion of the GM lesions show a strict respect for the GM/WM boundary. This contrasts with studies using histochemical staining techniques which suggest that multiple sclerosis lesions display a total disregard for anatomical boundaries.
Conclusion: We use myelin protein immunohistochemistry to demonstrate that GM demyelination is more extensive than WM demyelination throughout the spinal cord. We report novel patterns of GM demyelination that suggest pathogenetic differences between GM and WM lesions.

010 A PRESSING SITUATION – A CASE SERIES

O. R. Pearson, J. A. Johnston, S. Sadiq, M. Hourihan, N. P. Robertson. *Department of Neurology, Cardiff University, Cardiff, Wales; Department of Radiology, University Hospital of Wales, Cardiff, Wales*

Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiological entity characterised by altered cerebral function and seizures accompanied by radiological evidence of posterior cerebral

vasogenic oedema. Its exact aetiology remains unclear but the diagnosis is usually made on the background of immunosupression or severe systemic illness. Clinical and radiological features of PRES were reviewed in a retrospective case series of 11 patients identified over an eight-year period and outcome evaluated.

Mean age at presentation was 33 (range12 to 62) and sex ratio of affected patients 1M:F2.75. Commonest presenting features were altered mental status (10), seizures (10), headaches (3), visual hallucinations (3) and visual field deficits (2). Associated co-morbidity included severe hypertension (7), haematological malignancy (6), immunosupression or chemotherapy (6), renal failure(3) and toxaemia of pregnancy(1). Cranial CT imaging was performed in 11 patients and magnetic resonanve imaging in 4. In all cases extensive non-enhancing low signal change was observed in posterior occipito-parietal white matter bilaterally on CT compatible with vasogenic oedema and there were compatible areas of hyperintensity T2 signal change on magnetic resonance.

Good recovery was seen in all patients in whom early diagnosis and treatment and/or removal of the underlying cause was achieved. Awareness of the clinical and radiological features of PRES together with prompt treatment may improve outcome and prevent permanent neurological deficit.

011 NEUROBORRELIOSIS IN THE SOUTH WEST OF ENGLAND

J. K. Lovett, P. H. Evans, N. J. Gutowski. *Department of Neurology, Peninsula Medical School, Royal Devon and Exeter Hospital, Barrack Road, Exeter, UK*

Lyme Disease is becoming more commonly diagnosed in the UK. Previous UK studies, which have included mostly New Forest cases, suggest that 15% have neurological disease. However, this proportion may vary across the UK, as it does across the world. Moreover, it may not be recognised and treated as quickly in other UK regions. Therefore, we studied cases in the South West of England, the UK region with the second highest prevalence of Lyme Disease.

Methods: We reviewed hospital and GP notes of all patients in the Royal Devon and Exeter Hospital catchment area with positive borrelia serology during a five-year period (2000–2004).

Results: There were 90 cases, of which 64% had tick bites. The commonest symptoms were erythema migrans (64%) and arthralgia/myalgia (27%). However, 22 (24%) had neurological symptoms: 14 had Bell's palsy (3 bilateral), 8 confusion or drowsiness, 4 meningism, 5 radiculopathy, 2 other cranial nerve palsies, and 2 acute peripheral neuropathies. Of these 22 cases, treatment varied and the median delay from onset of symptoms to treatment was 26 days.

Conclusions: The proportion of Lyme patients with neuroborreliosis was higher than in previous UK Lyme studies. Cases should be identified and treated earlier.

012 CEREBROSPINAL FLUID OPENING PRESSURE IN ADULTS WITH ACUTE NEUROLOGICAL SYMPTOMS: REFERENCE INTERVAL AND INFLUENCE OF BODY MASS INDEX

W. Whiteley, R. Al-Shahi, C. P. Warlow. *Department of Clinical Neurosciences, Western General Hospital, Edinburgh, Scotland*

Background: We aimed to (1) measure the reference interval for CSF opening pressure in adult outpatients with neurological symptoms and (2) assess the relationship between body mass index (BMI) and CSF opening pressure.

Methods: We identified 354 adults in our neurology day unit database who had had prospective measurements of CSF opening pressure,-weight and height. We excluded patients who could have had raised or lowered intracranial pressure. We identified a sample of 242 patients; 108 male (45%), mean age 45, median body mass index 26 kg/m^2 (range 13–52 kg/m^2), all with axial brain imaging. They had a range of diagnoses reflecting outpatient neurology.

Results: The mean opening pressure was 17.2 cm of CSF with a 95% reference interval of 10–24.5 cm of CSF. Although the relationship between BMI and CSF opening pressure was statistically significant (Kendall's tau b = 0.32, 95% CI = 0.25 to 0.39), the relationship was not strong enough to be relevant to clinical practice.

Conclusions: (1) The upper limit of CSF opening pressure in patients without symptoms of raised intracranial pressure is higher than is usually quoted, and can be up to 28 cm CSF; (2) There is only a weak relationship between BMI and CSF opening pressure.

013 A CONTROLLED TRIAL OF SPECIFIC VISUAL REHABILITATION THERAPY IN PATIENTS WITH HEMIANOPIC ALEXIA

A. P. Leff, G. Spitsyna, S. A. McDonald, G. T. Plant, R. C. Shillcock, R. J. S. Wise. *National Hospital for Neurology and Neurosurgery and University College London, London, UK; Department of Clinical Neurosciences, Royal Free Hospital and University College Medical School, London, UK; MRC Clinical Sciences Centre and Division of Neuroscience, Faculty of Medicine, Imperial College, Hammersmith Hospital, London, UK; Department of Psychology, University of Edinburgh, Edinburgh, Scotland; Department of Neuro-ophthalmology, Moorfields Eye Hospital, London, UK*

Patients with an acquired right-sided homonymous hemianopia often complain of persistent text reading problems (hemianopic alexics (HA)); they lack essential visual information from their right visual field to help guide efficient reading scanpaths. Our hypothesis was that a specific visual rehabilitation method aimed at improving reading saccades would improve both reading speeds and scanpaths in a group of HA when compared to a sham visual rehabilitation therapy. Eighteen patients with HA were entered into two groups: one practiced with specific reading tapes daily for eight weeks (tapes group) while the other had sham therapy (spot-the-difference group) for four weeks and then crossed-over to tapes for a further four weeks. The tapes group showed significant improvements in text reading speed (repeated measures ANOVA, $p = 0.015$: size of effect 18% improvement), while the sham group did not improve over the first period (spot-the-difference therapy, $p = 0.138$) but did when they crossed over to the tapes ($p = 0.007$: size of effect 23% improvement). Measures of eye-movement behaviour were also commensurate with this behavioural improvement. This is the first study to demonstrate the effectiveness of a specific behavioural eye-movement based therapy in hemianopic alexia in the context of a controlled trial.

014 THE DYNAMICS OF A NEUROLOGY OUT-PATIENT SERVICE

G. Fuller. *Department of Neurology, Gloucestershire Royal Hospital, Gloucestershire, UK*

What do neurologists do in out-patients?

We conducted survey of neurology out-patients in a Neurology Service based at a District General Hospital over 12 weeks, looking at both new and follow up patients. 760 new and 1331 follow up patients were seen.

The range of new diagnoses was similar to previous series, with headaches (14%), migraine (10%) and epilepsy (12%) being most common reasons for referral. Other diagnoses included: movement disorders (6%), stroke and TIA (6%), neuropathies (5%), multiple sclerosis (4%), peripheral neuropathies (3%). About half the patients were discharged after the first consultation, either directly or following tests, 50% at the first review, 20% at the second review, 9% after 5–8 reviews and 5% after 9 or more. Epilepsy (37%), multiple sclerosis (17%) and Parkinson's disease (10%) and other movement disorders (7%) together accounted for two thirds of follow ups.

Conclusion: The neurology out-patient service consists of two interlinked services: a consultation service, that makes up 84% of new patients and 24% of follow ups, and a chronic disease management service that makes up 16% of new and 76% of follow ups. Better understanding the dynamics of neurology out-patients will enable rational planning of neurology services.

015 EXPERIENCE AS AN ACUTE LIAISON NEUROLOGIST: A NOVEL POST TARGETED AT THE ''COALFACE''

E. M. Dunn. *Department of Neurology, Leeds Teaching Hospitals, Leeds, UK*

Background: Patients presenting acutely with a neurological problem are often admitted to a Medical Assessment Unit (MAU). Neurological consultation on the MAU is by no means novel, but funding a new consultant neurology post for this purpose from MAU resources certainly is. Detailed audit of this innovative service at the LGI was encouraged by the trust (Leeds Teaching Hospitals), and supported with IT resources.

Methods: 100 acute neurological cases entered onto a dedicated access database – 50 referred prior to the commencement of the new service in October 2004 and the first 50 referred thereafter.

Results: Median time (days) from admission to referral reduced from 2 to 1, and median length of stay reduced from 8 to 6 days. Rates of imaging by CT and MRI did not alter, but earlier consultation led to better use of MRI with the new service. Examples include the diagnosis of compressive

lesions of the spinal cord (two cases) and cauda equina (one case), all three not suspected by the MAU team.
Conclusions: The job is enjoyable and rewarding, with time to teach acute neurology. The new service improves quality of care and makes financial sense through a reduction in length of stay.

016 THE NSF FOR LONG TERM CONDITIONS – DON'T BELIEVE THE HYPE!

A. J. Wills. *Queen's Medical Centre, Nottingham, UK*

The NSF for long-term conditions includes 11 quality requirements, of which two, focus on early diagnosis and emergency management. It has been claimed that this NSF is ''different'', with less emphasis on targets. However, the public-service agreement, which forms a part of the NSF, aims to reduce emergency bed days by 5% and prescribes an 18-week period from referral to treatment (including all tests). The small numbers of neurologists in the UK coupled with increasing reticence by other specialists or GPs to confidently diagnose neurological disease will undoubtedly cause this part of the NSF to fail. The advent of choose and book will probably not solve this problem because even well designed patient pathways or protocols are no substitute for clinical acumen. This has already been demonstrated by audits of the cancer 2 week wait system, which has been moderately successful in reducing waits for patients with GI or respiratory malignancy but has proved inappropriate in patients with ''neurological'' cancers. The advent of ''new'' ways of working (GPSIs or clinical networks) will not be a cost-effective solution; what is needed is an expansion in consultant numbers coupled with flexible job planning to improve efficiency and maintain a high-quality service.

017 A MYOCLONUS-DYSTONIA KINDRED. GENETIC DIAGNOSIS AND PROGRESS IN THE CONDITION OVER 10 YEARS

N. Cutfield, P. Cooper, K. Snow-Bailey, J. Dick, D. Prosser, J. Clayton-Smith, S. Sawcer, A. Compston, R. Roxburgh. *Neurology Department, Auckland City Hospital, Auckland, New Zealand; Neurology Department, Hope Hospital, Salford, UK; Lab Plus, Auckland City Hospital, Auckland, New Zealand; Genetics Department, St Mary's Hospital, Manchester, UK; Neurology Department, University of Cambridge, Cambridge, UK*

Myoclonus-dystonia, an autosomal dominant condition is largely a benign condition manifesting generally with non-progressive combination of fast myoclonic jerks and dystonic posturing. We present here a family in which three generations are affected. A video of four family members shows how different family members may be affected with more or less of these two movement disorders.

A follow-up video after ten years shows the progression of the disease. This demonstrates that the condition is not always benign in that one of the family members required a PEG – the first time this has been reported.

Sequencing the epsilon sarcoglycan gene led to the finding of a Stop mutation which has previously been reported as causing this disease. We discuss the implications of this for the family.

018 CHARACTERISATION OF ANTI-GAD ANTIBODIES IN STIFF-PERSON SYNDROME

T. Chang, P. Brown, A. Vincent. *Neurosciences Group, Weatherall Institute of Molecular Medicine, John Radcliffe Hospital, Oxford, UK; Sobell Department of Motor Neuroscience, Institute of Neurology, Queen Square, London, UK*

Stiff-person syndrome (SPS) is a highly disabling acquired neurological disease characterised by muscle rigidity with superimposed episodic muscle spasms. Autoantibodies to glutamic acid decarboxylase (GAD), the enzyme that synthesises the inhibitory neurotransmitter GABA, are detected in 60–80% of patients with SPS, but it is not clear whether these antibodies (Ab) are pathogenic.

Sera from 20 SPS patients were studied, comparing with 4 patients with type1 diabetes. GADAb titres ranged from 405 to 700 000 U/ml in 13 SPS patients. There was no correlation with the age of the patient or the duration of the illness. There was no significant difference in the GADAb titre between SPS patients who had received immunotherapy and those who had not. The antibodies were of high affinity and predominantly IgG1 isotype. In 3 of the 20 SPS patients, immunohistochemistry suggested the presence of CNS-directed autoantibodies in addition to GADAb, and flow cytometry showed that some of the SPS sera contained antibodies that could bind to the surface of neuronal cell lines.

GAD antibodies possess the characteristics expected of highly pathogenic autoantibodies, but GAD is an intracellular antigen. Some patients may have, in addition, antibodies to cell surface determinants that could be pathogenic.

019 THE ROLE OF NERVE GROWTH FACTOR IN PAINFUL NEUROMAS AND THE MECHANISM OF PAIN RELIEF BY THEIR RELOCATION TO MUSCLE

D. Atherton, O. Taherzadeh, P. Facer, D. Elliot, P. Anand. *Peripheral Neuropathy Unit, Division of Neuroscience and Mental Health, Imperial College London, UK; Hammersmith Hospital, London, UK*

Painful neuromas have been treated successfully by a number of surgical procedures, including relocation to muscle or bone, but the underlying molecular mechanisms of these procedures remain unclear. Nerve growth factor (NGF) is secreted by tissues and promotes the expression of sodium channels and other key molecules in sensory neurones which are involved in the generation and transmission of pain. We hypothesised that painful neuromas result from increased NGF levels, and that the efficacy of surgical procedures results from relative deprivation of NGF i.e. translocation of painful neuromas from NGF-rich regions, particularly cutaneous and sub-cutaneous structures associated with injury or inflammation, to NGF-poor structures such as muscle or bone. Using immunohistochemical methods, we have compared NGF to neurofilament ratios in painful distal upper limb neuromas excised during relocation procedures. NGF to neurofilament ratios were significantly elevated in painful neuromas ($n = 13$) in comparison to control nerves ($n = 6$, $p = 0.0004$). Previously painful neuromas relocated to muscle with complete pain relief ($n = 4$) demonstrated NGF to neurofilament ratios similar to those of the control nerves, and were significantly reduced compared to painful neuromas ($p = 0.005$). NGF levels may provide a molecular explanation for pain in neuromas, and the efficacy of relocation to muscle.

Case presentations

020 A KILLER OF A HANGOVER

A. Salek-Haddadi, P. Rangi, D. Johnson, J. Stern. *Department of Neurology, Atkinson-Morely Wing, St George's Healthcare NHS Trust, London, UK*

Following a hangover, a 52-year-old van driver presented with a one week history of shuffling gait, hiccupping, diplopia and somnolence. Over the next month, frontal headaches, difficulty judging distances, irritability, unsteadiness and incontinence followed culminating in a DGH admission. Initial bloods were unremarkable but MRI brain revealed high signal in the thalami bilaterally. Lumbar puncture showed raised protein (1.39 g/l) with normal cytology.

Upon transfer to the regional unit, he was disorientated and displayed utilisation behaviour with frontal release signs. His speech was incomprehensible and there was a ''thalamic astasia'' of gait (see video). Following an unchanged lumbar puncture with negative virology and repeat MRI, he underwent cerebral angiography. This revealed a large vascular malformation with multiple anterior and posterior circulation feeders together with an absent straight sinus. The patient suffered a fatal intracerebral haemorrhage before intervention could be embarked upon. Post-mortem revealed an even more widespread vascular malformation. There was no evidence of infection or encephalitis.
Conclusion: The radiological appearance of isolated thalamic hyperintensity carries a limited differential. Deep venous congestion second to AVM is rare but a potentially-treatable cause which clinicians and radiologists should recognise.

021 STIFF PERSON PLUS SYNDROME AND VOLTAGE GATED POTASSIUM CHANNEL ANTIBODY ASSOCIATED COGNITIVE IMPAIRMENT: NEW EVIDENCE FOR AN ASSOCIATION?

C. McGuigan, C. Buckley, T. Chang, A. Vincent, E. Everitt. *Department of Neurology, St. Mary's Hospital, Praed Street, London, UK; Department of Neuroimmunology, University of Oxford, Oxford, UK; John Radcliffe Hospital, Oxford, UK*

A 29-year-old African man was referred with a 3-year history of nocturnal tonic-clonic seizures. Three months prior to presentation he

noticed increasing unsteadiness, vertigo and spasms in his abdominal muscles. His mood had been low and his thinking less clear.

Examination revealed prominent down beating nystagmus in all directions of gaze. He had rigidity of abdominal and paraspinal muscles and increased tone in both lower limbs. He walked with a wide-based, ataxic gait. Mild cognitive impairment was confirmed on neuropsychometric examination. His HIV status was negative and thorough investigation did not identify any underlying neoplasm.

A clinical diagnosis of Stiff Person Syndrome (SPS) was confirmed on paraspinal EMG examination. Anti Glutamic Acid Decarboxylase antibodies (anti-GAD) were elevated in serum (150 000 units) and CSF. Voltage Gated Potassium Channel Antibodies (VGKCA) were also elevated (322pM).

The patient received one course of plasma exchange and subsequently intravenous immunoglobulin. He was commenced on high dose oral prednislone and azathioprine. After three months no clinical improvement had occurred. His autoantibodies remained elevated. Rituximab has been commenced.

The phenotype of VCKCA/GAD associated neurological disease continues to expand. This interesting identification of anti-GAD and VGKCA simultaneously in the same patient may suggest a common immunogenic mechanism.

022 OPSOCLONUS-MYOCLONUS ASSOCIATED WITH BENIGN OVARIAN TERATOMA. A CASE REPORT AND LITERATURE REVIEW

A. Fitzpatrick, O. M. Gray, G. V. McDonnell. *Department of Neurosciences, Royal Victoria Hospital, Belfast, Northern Ireland*

Background: Opsoclonus-myoclonus is characterised by nonrhythmic involuntary ocular oscillations, axial and segmentary myoclonia and cerebellar ataxia. It can be idiopathic, post-infectious or paraneoplastic, most commonly associated with neuroblastoma in children and lung or ovarian malignancy in adults.
Case Report: We report a 16-year-old-girl who presented with subacute onset of opsoclonus and myoclonus. She was ataxic rendering her bed dependant, nauseated and vomiting requiring nasogastric feeding. Examination revealed involuntary, chaotic eye movements and myoclonic jerks of all four limbs. Investigation excluded ongoing or recent infection, neuroblastoma and chest malignancy but revealed a right sided benign ovarian teratoma. Anti-neuronal antibodies were negative. The patient improved on treatment with clonazepam, immunomodulatory treatment including steroids and intravenous immunoglobulins and subsequent surgical removal of the teratoma. Video images before and after treatment will demonstrate this.
Discussion: Considering the significant response to tumour removal we discuss opsoclonus-myoclonus syndrome as a paraneoplastic manifestation of benign ovarian teratoma. Case reports suggest a variety of neurological paraneoplastic manifestations of this tumour but the association with opsoclonus-myoclonus has never been reported. We discuss the current evidence for optimal treatment with the low incidence of this condition precluding large randomised controlled trials.

023 ''THE WOMAN WHO MISTOOK THE PAST FOR THE PRESENT.'' A ''VARIANT'' PRESENTATION OF AN OLD DISEASE: A FURTHER DIFFERENTIAL FOR THE ''PULVINAR SIGN''

T. S. Monaghan, D. T. Murphy, M. Hutchinson, N. Tubridy. *St Vincent's University Hospital, Elm Park, Dublin 4, Ireland*

The case is presented of a 41-year-old female surgical patient who was transferred to our care with an amnestic syndrome associated with ataxia and ophthalmoplegia. This followed a complicated surgical course over an extended period with abdominal pain, vomiting, adhesions, ileus and parenteral nutrition.

Wernicke-Korsakoff syndrome was suspected. Certainty regarding the diagnosis was complicated by lack of information regarding the thiamine content of ''total parenteral nutrition'' administered to the patient. An alternative diagnosis of Creutzfeldt-Jakob Disease with important quarantine implications had to be considered due to neuroradiological abnormalities demonstrated on magnetic resonance imaging affecting the medial pulvinar as well as prominent neuro-psychiatric features common to both disorders. Creutzfeldt-Jakob disease has previously been misdiagnosed as Wernicke-Korsakoff syndrome.

Wernicke-Korsakoff syndrome is an important under-reported differential diagnosis for the ''pulvinar sign''. ''Total parenteral nutrition'' is a dangerous misnomer as not all preparations contain total requirements of vitamin supplementation.

024 GREETER'S CRAMP

S. H. Wong, P. J. W. McKee. *James Cook University Hospital, Middlesbrough, UK*

We present an interesting focal task-specific dystonia in our patient who works as a supermarket customer greeter. She develops an unusual puckering of her lips which only occurs on speaking (shown on video). Initially, touching the corner of her mouth acted as a ''sensory trick'' although this became ineffective with time as her dystonic symptom progressed. Apart from this movement disorder which occurred only on speaking, the rest of her examination was normal. An extensive battery of investigations has been normal including MRI brain, DAT scan, caeruloplasmin studies, ASOT, DYT1 gene and autoantibodies. Interestingly she seemed to improve subjectively after apomorphine and a subsequent therapeutic trial of levodopa. Focal task-specific dystonia such as specific context-related use of speech (auctioneering or praying) or embouchure dystonia have been described. However it appears that this unusual focal task-specific dystonia, which causes the puckering of lips on speaking, has not been previously described. In view of our patient's occupation, we call it a ''greeter's cramp''. The apparent partial response to dopaminergic agents is interesting.

025 THE CASE OF THE RHONDDA NEUROTOXIN: WESTERN GREEN MAMBA ENVENOMATION IN THE WELSH VALLEYS

R. Hocking, S. Malek, A. Lowman, M. D. Page, J. Murray, T. P. Pickersgill. *Departments of Medicine and Orthopaedics, Royal Glamorgan Hospital, Pontypridd and Rhondda NHS Trust, Llantrisant; Department of Neurology, University Hospital of Wales, Cardiff and Vale NHS Trust, Cardiff*

A 36-year-old amateur ophiologist sustained a Western Green Mamba snake bite at 18:45 h to his left hand. He tightly bandaged the arm and arrived in the A&E department at 19:35. He was haemodynamically stable and neurological examination was unremarkable. He was admitted to the Intensive Care Unit for observation. At 20:45 the patient complained of parasthesiae in his face and limbs. The patient received snake-specific antivenom and his neurological symptoms subsided.

A fasciotomy was subsequently performed due to acute compartment syndrome affecting his carpal tunnel and flexor forearm compartments.

Green Mamba snake venom contains neurotoxins including muscarinic toxins and dendrotoxins. Neurological sequelae may include ptosis, opthalmoplegia, bulbar or generalised weakness, respiratory failure and parasthesiae. Systemic effects include shock, abdominal pain, vomiting and coagulopathy.

The patient reports that there are 25 registered keepers of venomous snakes in the UK but suspects there are a further 500 with venomous snakes at home who are not registered. We may see an increase in the number of snake envenomations in humans in the UK and need to be aware of the neurological sequelae and the availability of antivenom.

Posters

026 PARANEOPLASTIC CRANIAL NEUROPATHY IN ASSOCIATION WITH ANTI-HU (ANNA-1) ANTIBODY

T. P. Harrower, J. Dixon, S. Catania, D. G. O'Donovan, R. N. De Silva. *Department of Neurology, Essex Centre for Neurological Sciences, Oldchurch Hospital, Romford, UK*

Paraneoplastic neurological disorders in association with anti-Hu antibody include cerebellar degeneration, limbic encephalitis, sensorymotor polyneuropathy, dorsal root ganglionitis, autonomic neuropathy and myelitis. Two subjects with small-cell lung carcinoma (SCLC) and anti-Hu antibody, who presented with progressive deafness and multiple cranial palsies, are described.

A 50-year-old woman, presented with progressive deafness, abdominal pain and ataxia. Audiometry and brainstem evoked potentials revealed bilateral sensori-neural deafness. MRI of the brainstem was normal. At autopsy cochlear spiral ganglionitis was demonstrated. Case 2, a 67-year-old woman presented with right trigeminal, bilateral abducens and right facial nerve palsies. She also had a right Adie pupil, right senisori-neural deafness and cerebellar incoordination. Contrast-enhanced MRI of the brain and repeated cytological examinations of the CSF were normal. Combination chemotherapy for biopsy-proven SCLC has resulted in partial recovery of cranial nerve function.

Cranial neuropathy as a paraneoplastic syndrome may be under-recognised. Review of the literature revealed one previous case of autopsy-confirmed cochlear spiral ganglionitis. There have been 4 previous cases of multiple cranial nerve palsies associated with anti-Hu and SCLC. Deafness, unexplained ataxia and autonomic dysfunction may be helpful ''red flags'' which may lead to earlier diagnosis of SCLC, and possibly better outcome.

027 FROM THE DEPARTMENT OF NEURO-DERMATOLOGY: IS BRACHIORADIAL PRURITUS A CENTRAL NEUROLOGICAL DISORDER?

J. A. Johnston, O. R. Pearson, T. P. Pickersgill, R. Logan. *Department of Neurology, Cardiff and Vale NHS Trust, University Hospital of Wales, Cardiff, Wales; Department of Dermatology, Bro Morgannwg NHS Trust, Princess of Wales Hospital, Bridgend, Wales*

Brachioradial pruritus is a clinical entity of localised and severe itching classically affecting the skin on the radial side of the forearms and lateral aspect of the upper arms. It is historically described as ''tropical dermopathy'' or ''solar pruritus of the elbows'' and it's cause is controversial.

The condition has a more complex aetiology than purely photosensitivity and recent evidence points towards it being a photo-neurological disorder involving cervical spine disease or peripheral nerve damage.

We describe a 45-year-old female, who presented with a 5-year history of intensely itchy forearms, between the months of September and February. Examination did not demonstrate any abnormality except for brisk knee and ankle reflexes. Magnetic resonance imaging of the cervical spine demonstrated an unusual high signal central cord lesion at C7. CSF constituents were normal.

We postulate that this solitary lesion at C7, which might be a cavernoma, may be responsible for her condition. In light of this we review the evidence and discuss that brachioradial pruritus is not purely a result of chronic sun exposure, but may indeed represent an underlying neurological problem, demonstrating the need for neurological assessment, investigation, and a close working relationship between the disciplines of dermatology and neurology.

028 MOBIUS SYNDROME WITH ASSOCIATED REM SLEEP BEHAVIOUR DISORDER

K. N. Anderson, G. G. Lennox, I. Smith. *Department of Neurology, Addenbrooke's Hospital, Cambridge, UK; Respiratory Support and Sleep Centre, Papworth Hospital, Cambridge, UK*

Mobius syndrome is a congenital cranial dysninnervation disorder that characteristically causes bilateral sixth and seventh cranial nerve palsies as well as a range of other skeletal abnormalities. It is thought to be due to a failure of development of the rhombencephalon with associated posterior fossa and brainstem abnormalities.

We present a case of Mobius syndrome with associated sleep disturbance that had been present from birth. The patient described stereotyped violent dreams with dream reenactment that had caused self injury. The symptoms were resistant to numerous treatment strategies including Clonazepam and anticonvulsants. Brain imaging and 12 lead electroencephalogram were normal and video polysomnography demonstrated abnormal behaviours during the second half of the night. The polysomnography was particularly difficult to interpret in the context of the patient's Mobius syndrome. REM sleep is defined not only by EEG activity but also by chin tone EMG and roving eye movements, both of which were absent.

There is an association with obstructive sleep apnoea and Mobius syndrome secondary to palatal abnormalities. Abnormal development of brainstem structures, in particular the pons, might predispose patients with Mobius syndrome to REM sleep behaviour disturbance but there is only a single other case reported with this association.

029 MYOCLONIC ATAXIA AND OPTIC ATROPHY: PHENOTYPIC VARIABILITY IN AOA2

N. P. Davies, V. Srinivasan, A. M. R. Taylor. *Birmingham Muscle and Nerve Centre and Institute of Cancer Studies, University Hospital Birmingham NHS Trust, Birmingham, UK*

Background: Myoclonic ataxia (Ramsay Hunt syndrome) can be caused by several genetic and acquired conditions including mitochondrial disorders and coeliac disease. To date, a presentation with myoclonic ataxia with or without optic atrophy has not been described in ataxia ocular motor apraxia type 2 (AOA2). Here we describe the first AOA2 family presenting in this way and review the differential diagnoses of the recessive ataxias

Patients: Three siblings (age 27, 24 and 18) were initially seen with a clinical label of Ramsay Hunt syndrome. Each had presented with myoclonic ataxia of varying degrees. Additional features such as peripheral neuropathy, ophthalmoparesis and optic atrophy showed intra-familial variability. Screening tests for causes of myoclonic ataxia were negative.
Results: Blood alphafetoprotein levels were elevated but DNA fragility tests were normal. Western blot analysis demonstrated an absence of the senataxin protein confirming the diagnosis of AOA2. This was supported by the identification of mutations in the senataxin gene.
Conclusion: AOA2 is at least as common as ataxia telangiectasia and can present with myoclonic ataxia and optic atrophy. When faced with a recessive ataxia, simple tests such as serum albumin and alphafetoprotein can be pivotal in directing genetic analysis.

030 NEURAL CONTROL OF VOLUNTARY BREATHING: INSIGHT FROM FUNCTIONAL NEUROIMAGING

B. Koritnik, C. M. Andrew, S. C. Williams, P. N. Leigh. *King's College London, Institute of Psychiatry, London, UK*

The neural control of breathing consists of a central drive to the respiratory muscles, which is modulated by sensory, behavioural and emotional influences (automatic, voluntary and emotional breathing, respectively). In recent years, functional magnetic resonance imaging (fMRI) has been used to study voluntary breathing. The studies found consistent bilateral activations predominantly in the primary sensorimotor cortex, lateral premotor cortex, supplementary motor area and cerebellum.

We have used fMRI in healthy subjects performing a sniff manoeuvre in an event-related design. Nasal pressure and chest movements were measured continuously. Image analysis was performed using SPM2 software.

A bilateral cortical sensorimotor network was found to be activated during the sniff manoeuvre, consisting of primary sensorimotor cortex (located medially to the hand area), lateral premotor cortex and supplementary motor area. Bilateral activations were also found in cerebellum, insula and basal ganglia.

It is feasible to use fMRI during the sniff manoeuvre to visualise the cortical sensorimotor network associated with control of voluntary breathing. The method offers the possibility to explore the neural control of breathing in healthy humans and in patients and therefore to explore cortical influences on respiratory function in neurological disorders such as ALS.

031 SHOULD WE TEST FOR CELIAC DISEASE IN PATIENTS WITH RELAPSING-REMITTING NEUROLOGICAL SYMPTOMS?

T. Mihalova, M. J. Stone, C. P. Hawkins. *Neurology Department, University Hospital of North Staffordshire, Stoke-on-Trent, UK*

A 48-year-old woman had attended the neurology department with relapsing-remitting neurological symptoms for 10 years. Her symptoms included fluctuating paraesthesia in her hands and feet, intermittent diplopia and progressive ataxia. From 1999 she had received iron replacement therapy for iron deficiency anaemia which was believed to be secondary to gynaecological problems. Repeated assessments showed fluctuating left sided dysmetria, subjective diplopia, positive Romberg's test, decreased pinprick sensation in right hand and gait ataxia. The following investigations were either normal or negative: serum B12, serum folate, electromyogram and nerve conduction studies, brain and cervical spine MRI, and visual evoked potentials. CSF analysis revealed systemic IgG synthesis. Although she had no abdominal symptoms autoantibodies for coeliac disease were requested in view of iron deficiency. We yielded positive anti-transglutaminase IgA, anti-endomysial antibodies and anti-smooth muscle antibodies. Endoscopy and duodenal biopsy confirmed the diagnosis of coeliac disease.

Various neurological sequelae of coeliac disease have been reported including epilepsy, peripheral neuropathy, diplopia and ataxia, but uncommonly with a relapsing-remitting pattern. The pathophysiology of the neurological disturbance is not completely understood, although the anti-gliadin antibodies crossing through the blood-brain barrier may play a role.

032 SUPERFICIAL SIDEROSIS: AN UNDER-RECOGNISED CONDITION

V. J. Verma, A. S. Al-Din. *Neurology Unit, Pinderfields General Hospital, Aberford Road, Wakefield, West Yorkshire, UK*

Superficial siderosis, a condition characterised by chronic haemosiderin deposition in the brain following recurrent subarachnoid haemorrhage,

is generally considered to be rare and is characterised by relentlessly progressive triad of bilateral deafness, cerebellar dysfunction and pyramidal signs. Causative mechanisms vary from post-surgical cases, trauma, vascular malformations, unrecognised recurrent subarachnoid haemorrhages and childhood cerebellar tumours. Until the advent of magnetic imaging, this condition was largely under-diagnosed with almost all the cases being reported from post-mortem studies. The MRI is a fairly sensitive tool in detecting the characteristic abnormalities and therefore has facilitated sensitive, safe and non-invasive diagnosis with considerable specificity. This can be supported by evaluation of the cerebrospinal fluid for ferritin, transferrin and siderophages. Site of bleeding can then be searched for, using MRA and sometimes formal angiography.

We present case histories of two patients. The first presented with predominantly unexplained sphincteric dysfunction with minimal long tract signs. The second presented with progressive spastic paraparesis and sphincteric dysfunction 35 years after successful surgical removal of a cervico-thoracic meningioma. Neither of them presented with the classical triad characteristic of superficial siderosis but both proved to have MRI changes typical of superficial siderosis. In both superficial siderosis was either the main or a significant contributing factor to the recent neurological dysfunction. Chelating agent (Trientine) was started in these cases in the hope to slow down disease progression.

We further discuss the need to consider superficial siderosis in the differential diagnoses in patients with unexplained neurological deficits like sphincteric dysfunction, hearing impairment and pyramidal or cerebellar signs.

033 GENETIC AND PATHOLOGICAL HETEROGENEITY OF FAMILIAL FRONTO-TEMPORAL DEMENTIA IN WALES: A STUDY OF 6 FAMILIES

M. M. Wickremaratchi, P. Momeni, J. Hardy, J. Neal, H. R. Morris. *Department of Neurology, Cardiff University, B2-C2 Link, University Hospital of Wales, Cardiff, Wales; Laboratory of Neurogenetics, National Institute on Ageing, Porter Neuroscience Building, Bethesda, MD20892, USA; Department of Pathology, University Hospital of Wales, Cardiff, Wales*

Background: Fronto-temporal dementia (FTD) is common in patients below the age of 65 years. About a third of cases are familial and a variety of genes are responsible, including tau (MAPT). Wales has been identified as the founder origin of the MAPT exon 10 + 16 mutation, a widespread cause of familial FTD.
Methods: A region wide survey of familial FTD in Wales has been initiated using secondary care referrals. Newer staining techniques have been applied to archived pathological samples from deceased family members and MAPT sequenced.
Results: Six FTD families have been identified and we describe their clinical features. All include fronto-temporal dementia and variable extra pyramidal features, including a Progressive Supranuclear Palsy (PSP) and asymmetric parkinsonism phenotype. The age at onset ranges from 28 to 48 years. Two families have tau mutations (exon 10 + 16 and S356T). Three families have non-tau FTD pathology, two of which have concurrent clinical motor neurone disease in some members. Pathological examination in one kindred shows characteristic intra-neuronal ubiquitin inclusions with cerebellar pathology.
Conclusion: The study of these families highlights the clinical, genetic and pathological heterogeneity of familial FTD apparent in the Welsh population.

034 PREVALENCE AND AETIOLOGY OF SEIZURES AT TIME OF CLINICAL DIAGNOSIS OF ALZHEIMER'S DISEASE

D. A. Lozsadi, A. J. Larner. *Walton Centre for Neurology and Neurosurgery, Lower Lane, Fazakerley, Liverpool, UK*

Objective: To investigate the prevalence and causes of epileptic seizures at the time of clinical diagnosis of Alzheimer's disease.
Methods/Setting: Observational study of all newly diagnosed Alzheimer's disease patients seen by one consultant neurologist at a regional Cognitive Function Clinic over a 5-year period (January 2000–June 2005 inclusive).
Results: Of 166 patients diagnosed with Alzheimer's disease (M:F = 78:88, age range 49–84 years), 10 (6%) had a history of seizures (M:F = 4:6, age range 58–76 years) four with Alzheimer's disease onset before age 65 years.

Of these 10, 4 had seizures judged unrelated to Alzheimer's disease (onset >10 years before cognitive decline), 2 with childhood onset primary generalised seizure disorders. Six patients had seizure onset contemporaneous with onset of cognitive decline, in 5 of whom no symptomatic cause for seizures other than Alzheimer's disease could be identified. Seizure type, as far as could be determined within the limits of memory decline, was partial in all five Alzheimer's disease-related cases, with secondary generalisation in three.
Discussion/Conclusion: Previous studies indicate that seizures become more prevalent with Alzheimer's disease progression, but this study shows that seizures may be present at time of diagnosis, and symptomatic, of Alzheimer's disease. Seizure type is similar to that encountered in later stages of disease.

035 ABCB1 POLYMORPHISMS AND HAPLOTYPE PREVIOUSLY ASSOCIATED WITH DRUG RESISTANT EPILEPSY HAVE NO EFFECT ON THERAPEUTIC OR ADVERSE DRUG RESPONSE IN A LARGE PROSPECTIVE EPILEPSY COHORT

G. Leschziner, A. Jorgensen, T. Andrew, C. Middleditch, M. Pirmohamed, P. Williamson, A. Marson, A. J. Coffey, J. Rogers, D. R. Bentley, D. Chadwick, M. R. Johnson. *Imperial College, London, UK; Wellcome Trust Sanger Institute, Cambridge, UK; University of Liverpool, Liverpool, UK*

P-glycoprotein, product of the ABCB1 gene and an active efflux mechanism for numerous antiepileptic drugs (AEDs), has been implicated as a putative mechanism of multidrug resistance in epilepsy. The C3435T polymorphism and/or a three-SNP haplotype have been reported to be associated with multidrug resistance in three previous retrospective studies, but a further two studies have failed to replicate these findings. Although retrospective case control designs are timely and cost-effective, choice of controls and non-standardised definitions of clinical outcomes may confound the detection of genes with modest effect size. To obviate concerns regarding retrospective design, we genotyped C3435T and the two other polymorphisms in a unique prospective cohort of 505 epilepsy patients. We found no evidence for an association of C3435T or haplotype with time to first seizure after initiation of AED therapy, time to twelve month remission, time to drug withdrawal due to unacceptable side effects or time to withdrawal due to lack of seizure control, using time-to-survival analyses. The study illustrates the considerable value of prospective epidemiological design in determining genetic effect size for clinically relevant outcomes, despite the significantly greater cost, time and manpower required to establish prospective clinical genetic resources.

036 PROSPECTIVE EPILEPSY DNA BANK: SANAD AND MESS LINKED DNA REPOSITORY

M. Johnson, J. Allen, M. Alwaidh, J. Andrews, R. Appleton, H. Arbery, D. Beck, R. Bennett, D. R. Bentley, P. Burt, P. Cleland, H. Cock, O. C. Cockerell, A. J. Coffey, P. N. Cooper, R. N. Corston, C. E. Cramp, P. Crawford, B. E. A. Dafalla, T. Esmonde, G. Fuller, J. Geldard, P. J. Goulding, E. Hawkins, F. Hinde, E. Howard, S. J. Howell, A. Hughes, M. Jackson, S. Jamieson, M. R. Johnson, M. W. Kellett, A. D. Kindley, R. Lauder, M. Lawden, G. Leschziner, J. Liddle, G. Litherland, S. Macdonald, A. G. Marson, L. McCoy, B. McLean, C. Middleditch, R. Newton, D. J. Nicholl, L. North, L. Owen, M. Parratt, P. Pirmohamed, M. Reuber, R. Roberts, J. Rogers, B. Sharrack, N. C. Silver, D. Smith, P. E. M. Smith, S. Steward, J. Stewart, C. Thompson, P. Tidswell, T. Von Oertzen, U. Weishmann, K. White, P. Williamson, D. Chadwick. *Imperial College London, London, UK; University of Liverpool, Liverpool, UK*

Association studies of genetic polymorphisms have been mostly performed in the retrospective case control setting. A troubling number of ''significant'' associations have been reported that could not be confirmed in later studies. A number of factors have been proposed to explain ''replication failure'', including publication bias, inadequate power, lack of adjustment for multiple testing, population substructure and genotyping failure and error. Less frequently considered are the inherent limitations of the retrospective epidemiological design. Although retrospective case control designs are time and cost effective, choice of controls, measurement error and non-standardised definitions of clinical outcomes may confound the detection of genes with modest effect size. To obviate concerns regarding the retrospective design, we have established a DNA bank based on two large-scale prospective cohort studies in epilepsy, the SANAD and MESS studies coordinated by Professor Chadwick. Utilizing the unique research network established to conduct these trials, we have collected over 800 DNA samples on new onset epilepsy patients whose clinical outcomes including drug response (both therapeutic and adverse) have been validated within prospective structures. This represents a national resource for the detection of genes and clinical factors and their joint interactions that inform clinical outcomes in epilepsy.

037 PROVISION OF INFORMATION FOR WOMEN WITH EPILEPSY: AN AUDIT OF PRACTICE

E. Stern, H. R. Cock. *Atkinson Morley Regional Neuroscience Centre, St Georges NHS Trust and St Georges, University of London, London, UK*

Introduction: During pregnancy both antiepileptic drugs and poorly controlled seizures carry risks. Some drugs also interact with hormonal contraceptives. We examined documentation of information provision to women with epilepsy at a regional centre, and the patient's recollection of this.
Methods: Retrospective, notes-based audit of 62 women aged 18–51 years presenting for follow-up. 30 of these women also completed a questionnaire.
Results: Most records documented that information had been provided on seizure risks during pregnancy (69.4%), teratogenicity (75.8%) and folate supplementation (64.5%). Women in the 25–35 age range were considerably more likely to have received this information than other women ($p = 0.004$). 56.7% of women taking enzyme-inducing medications had a record of being given information about possible interactions with oral contraceptives. Women first seen by a general neurologist waited significantly longer before first receiving pregnancy-related information than those first seen by epileptologists.
Discussion: The recently established epilepsy group is improving services, but despite active measures not all women appear to be receiving important information. There is a bias against giving information to women outside the ''core'' child-bearing age range, and information related to contraceptives is a relative weakness. This illustrates the need for systematic processes, and provides a focus for future improvement.

038 TODD, FARADAY AND THE ELECTRICAL BASIS OF BRAIN ACTIVITY

E. H. Reynolds. *Institute of Epileptology, King's College, Denmark Hill Campus, London, UK*

The origins of our understanding of the electrical basis of brain activity are usually associated with the names of Fritsch, Hitzig, Ferrier, Jackson, Caton and Berger. This overlooks the earlier contributions of Robert Bentley Todd (1809–1860), influenced by his contemporary in London, the great electrical scientist, Michael Faraday (1791–1867). Faraday was interested in animal electricity amongst all other forms of electricity (eg voltaic, galvanic), and undertook experiments on the electric eel (gymnotus) attended by Todd. Todd, who was Professor of Morbid Anatomy and Physiology at King's College, London, was the first to apply Faraday's concepts of the polar forces of electricity and magnetism to the brain. As a pioneer microscopist he brilliantly foresaw each nerve vesicle (cell) and its related fibres, ie neurone in later terminology, as a distinct apparatus, analogous to a battery, for the development and transmission of ''nervous polarity'' by unknown metabolic mechanisms; a concept that was confirmed a century later by the Nobel prize winning work of Hodgkin and Huxley. Todd also applied Faraday's concept of ''disruptive discharge'' to explain epileptic seizures, and he confirmed this experimentally in rabbits using Faraday's newly discovered electro-magnetic rotation machine.

039 VIGABATRIN IN UTERO: VISUAL ASSESSMENT USING STANDARD AND NOVEL TECHNIQUES

C. Lawthom, J. M. Wild, P. E. M. Smith. *Neurology Dept, University Hospital of Wales, Wales; School of Optometry and Vision Science, Cardiff University, Wales*

First reports of vigabatrin-attributed visual field loss (VAVFL) emerged in 1997. VAVFL is irreversible, and the gold standard for assessment is static perimetry. Optical Coherence Tomography of the peri-papillary retinal nerve fibre layer (RNFL) has previously demonstrated reduced RNFL thickness in individuals with VAVFL.

Only two cases have been published to date, each with one child exposed in utero. Results were indeterminate. We present the first visual investigation of an adult with VAVFL (mother (M) age 40 y) and her two daughters (aged 10 (D1) and 7 years (D2)) respectively exposed in utero.

Both children were delivered at term, with no malformations and were formula fed.
Results:
Conclusions: We report the first definitively normal visual field studies in individuals exposed to vigabatrin in utero, and the first sibling pair exposed in utero. The reduced RNFL thickness value observed in D1 is suggestive of sub-clinical dysfunction. We propose that visual surveillance of this group should be ongoing.

040 EVALUATING THE POTENTIAL ROLE OF GENERAL PRACTITIONERS WITH SPECIAL INTERESTS (GPWSIS) IN HEADACHE: A PRELIMINARY ASSESSMENT

L. Ridsdale, A. Dowson, J. Ferguson, T. Roberts, P. Seed. *Department of General Practice & Primary Care, Department of Neurology, King's College London, London, UK; Lambeth Primary Care Trust, London, UK*

Introduction: Headache is the commonest new neurological symptom seen by general practitioners (GPs) and neurologists. GPs refer 2–3% of patients with headache to specialists. Access to neurologists for all problems is poor. We aimed to describe workload in neurology outpatients in Lambeth and Southwark, and to train GPs in headache.
Methods: Guy's & St Thomas' and King's College Hospitals outpatient data were collected retrospectively for 2000–3, and prospectively for eight weeks in 2003–4. Southwark and Lambeth GPs were offered the opportunity to train in headache.
Results: Retrospectively there were 66 000 hospital neurology appointments; 32% were new referrals, 77% from GPs, 17% from consultants. Hospital clinicians discharged from 32% to 94% of patients after the first appointment. Prospectively we found 30% of new referrals were for headache. Four GPwSIs were trained. They are developing guidelines, visiting practices with an educational package, and running a pilot headache clinic.
Conclusions: GPs' decision-making largely determines the volume and mix of neurologists' new work, with 30% of new appointments for headache. GPwSIs can inform GPs about diagnosis and management for the 97% of headache patients they see without referral, and manage some of those referred in an intermediate care clinic. This will be assessed.

041 FUNCTIONAL MRI IN SUNCT (SHORT-LASTING UNILATERAL NEURALGIFORM HEADACHE ATTACKS WITH CONJUNCTIVAL INJECTION AND TEARING) AND SUNA (SHORT-LASTING UNILATERAL NEURALGIFORM HEADACHE ATTACKS WITH CRANIAL AUTONOMIC SYMPTOMS) SHOWS DIFFERENTIAL HYPOTHALAMIC ACTIVATION WITH INCREASING PAIN

A. S. Cohen, M. S. Matharu, R. Kalisch, K. Friston, P. J. Goadsby. *Headache Group and Wellcome Department of Imaging Neuroscience, Institute of Neurology, Queen Square, London, UK*

SUNCT and SUNA are rare Trigeminal Autonomic Cephalgias (TACs). Functional imaging studies have shown hypothalamic activation in TACs, and deep brain hypothalamic stimulation has proven beneficial.

Nine patients with primary SUNCT, one with SUNCT secondary to a brainstem lesion, and two patients with SUNA underwent functional MRI whilst experiencing attacks amongst attack-free periods. Pain levels were rated by pressing a keypad. The images were analysed with SPM2 (www.fil.ion.ucl.ac.uk/spm/). Brain activation in a region of interest in the hypothalamus was predicted to vary parametrically with pain ratings. Activated voxels are reported at $p<0.001$ uncorrected.

In primary SUNCT, of 6 patients with left sided attacks; 3 had right-sided and 3 had bilateral positive activations. Two patients with right sided attacks had right-sided negative activations; one with bilateral attacks had bilateral activation.

In secondary SUNCT there were no activations.

In SUNA, there were right-sided negative activations in one patient with right-sided and one with left-sided attacks.

Hypothalamic activation has been shown ipsilaterally, contralaterally and bilaterally in TACs. This study shows hypothalamic activation which increases with increasing levels of pain in primary SUNCT, although with negative activation in SUNA. It strengthens the role of the hypothalamus in the pathophysiology of TACs and poses questions about the basis for the laterality of the attacks.

042 MEDICATION-OVERUSE HEADACHE IN CLUSTER HEADACHE PATIENTS

A. Bahra, K. Paemeleire, S. Evers, M. S. Matharu, P. J. Goadsby. *Institute of Neurology, Queen Square, London, UK*

Medication-overuse headache (MOH) affects up to 2–3% of the population. There is evidence that MOH occurs in individuals who are predisposed to a primary headache disorder. Patients with migraine and tension-type headache comprise the majority of this patient group. Frequency rather than dosing of acute-relief medication appears to be crucial to the development of MOH. The mean time to development of MOH is the shortest for the Triptans, followed by ergotamine and thence

analgesics. Cluster headache is an uncommon and clinically distinct primary headache disorder. In episodic cluster headache the headache attacks typically occur daily, often several times, for several weeks or months at a time interspersed by periods of complete remission from pain. In chronic cluster headache the attacks can occur daily for at least a year without significant remission. The most effective acute-relief medication is subcutaneous sumatriptan. Despite twice daily (thus maximal) use of sumatriptan in chronic cluster headache MOH is not reported in patients with cluster headache. We report a group of patients with cluster headache and MOH. The data support previous literature that those patients who develop MOH may be a subgroup who also have a genetic predisposition to migraine.

043 PROSPECTIVE AUDIT OF A NURSE-LED HEADACHE SERVICE IN A SUBREGIONAL NEUROLOGY UNIT

C. E. Clarke, J. Edwards, D. Nicholl, A. Sivaguru, P. Davies. *Department of Neurology, Sandwell and West Birmingham NHS Trust and University of Birmingham, Birmingham, UK*

Headache is one of the most common presentations to neurology outpatients. The UK shortage of neurologists causes long waiting times for appointments, short consultations, and poor follow up to monitor and adjust treatment.

We performed a prospective audit of the introduction of a nurse-led headache service in a subregional neurology unit.

The nurse was trained to diagnose migraine and tension-type headache and advise GPs on treatment and to collaborate with consultants in evaluating other types of headache.

The service produced a 29% reduction in waiting time for headache patients and 35% reduction in the general neurology waiting time. Patients waiting more than 13 weeks were abolished. The majority of patients had tension-type headache (45%) and migraine (43%). The proportion of patients requiring neuroimaging fell from 29% to 13%. Patients who returned to a first follow up appointment had 0.84 unit improvement in headache severity on a 7 point Likert scale (−3 to +3).

A nurse led headache service can safely and effectively treat simple headache disorders leading to reduced waiting time for all neurology patients and less neuroimaging. Expansion of the service nationwide should lead to an improved service for patients with neurological disorders.

044 HOW DO WE MANAGE REFERRAL NUMBER?

P. K. Morrish. *Royal Sussex County Hospital, Brighton (or Gloucestershire Foundation Hospital Trust), UK*

Introduction: To provide a comprehensive neurology service in a target-driven and resource-limited health service it is helpful to understand referral pattern. Data are presented from a five-year investigation into new patient referrals.
Method: The number and origin of referrals was assessed between 1999 and 2003. Personal referral number was returned to GPs (comparing with colleagues) and comment invited. GPs were also asked the reason for referral, whether the referral was GP or patient-instigated, and whether alternatives to referral might be acceptable. GPs and consultant neurologists rated referrals from high and low referrers for appropriateness.
Results: New patients seen increased from 1393 in 1999 to 1938 in 2003 as median wait dropped, from 156 days in 2000 to 67 days in 2003. The majority of GPs welcomed referral information. 25% of referrals were patient-instigated. 32% of new patient referrals might be managed instead by direct access to investigation. There was no significant difference in appropriateness of referral from high and low referring GPs, and no inter-rater difference in appropriateness.
Conclusions: New referrals have risen beyond an increase in neurological disease, and enforced prioritisation of new patients risks disadvantage to the chronically ill. GPs are amenable to dialogue concerning referral practice.

045 NEUROLOGISTS BEWARE! DOES YOUR TEAM HAVE A LONE WORKER POLICY?

G. Clayton, L. E. Coates, T. P. Pickersgill, N. P. Robertson. *Cardiff and Vale NHS Trust, Cardiff, Wales; Cardiff University, Cardiff, Wales*

Multidisciplinary team working is commonplace in neurological practice, particularly in the management of chronic disorders. The last few years has seen a large increase in numbers of Clinical Nurse Specialists (CNS) directly involved in both hospital and community management of patients with conditions such as multiple sclerosis, Parkinson's disease and motor neurone disease.

It is now customary for many aspects of symptom management, counselling and needs assessments to be undertaken by the CNS in the patient's own home. A number of adverse incidents involving hazardous or threatening environments led us to the conclusion that a proactive approach to safety was necessary.

We routinely offer home visits for all patients newly diagnosed with multiple sclerosis, and many patients are seen for community rehabilitation interventions. As the team has grown, the number of home visits and hence risk of further critical incidents has also grown.

We describe the development of a ''Lone Worker Policy'' tailored to the needs of our multiple sclerosis team. This uses the concept of a nominated person responsible for ensuring the safety of staff on home visits and maintaining contact; and gives specific advice on danger awareness, risk minimisation and communications.

We recommend that neurologists should recognise the importance of the safety of team members who undertake home visits and be proactive in developing similar policies.

046 THE BURDEN OF MONOGENIC NEUROGENETIC DISORDERS IN GENERAL NEUROLOGICAL PRACTICE

A. J. Larner. *Walton Centre for Neurology and Neurosurgery, Lower Lane, Fazakerley, Liverpool, UK*

Objective: To measure the frequency of monogenic neurogenetic disorders in general neurological practice.
Methods/Setting: Observational study of new, follow-up, and ward consultations seen at two district general hospitals and a regional neuroscience centre by one consultant neurologist (excluding specialist interest dementia clinic) over a six-year period (2000–2005 inclusive).
Results: From approximately 6000 new, 3000 follow-up, and 1000 ward consultations, forty-six patients with fourteen monogenic neurogenetic disorders were identified. The most common conditions seen were Huntington's disease (HD; 12) and neurofibromatosis (NF; 11); a further eleven patients had seven different neuromuscular disorders (facioscapulohumeral dystrophy and hereditary motor and sensory neuropathy most common); the remaining twelve had five other diagnoses. More than one family member affected with the same neurogenetic disease occurred on four occasions (HD twice, X-linked adrenoleukodystrophy, Friedreich's ataxia). All consultations related to diagnosis or management of the neurogenetic disorder with the exception of five ''incidental'' NF cases. Overall, 21 cases were new diagnoses, 25 had established diagnoses at time of referral or follow-up. Eighteen patients underwent neurogenetic testing, but only six of these tests were requested by the neurologist.
Discussion/Conclusions: The burden of monogenic neurogenetic disorders seen in general neurological practice is small: approximately three new diagnoses and one positive neurogenetic test per year. These observations have implications for trainee teaching about neurogenetic disorders, and for training in taking informed consent for genetic testing.

047 WHAT DO DAY CASE PATIENTS REALLY KNOW ABOUT LUMBAR PUNCTURE?

M. D. Cossburn, V. Wilson, J. Gorst, S. Hadjikoutis. *Department of Neurology, Morriston Hospital, Swansea, Wales*

Lumbar puncture (LP) is routinely performed on neurology wards and is increasingly being performed as a ''day case''. We undertook to ascertain what patients attending for day-case LP understood about their procedure.

Two self-administered questionnaires were given to patients. The first to be completed on arrival, the second post procedure. Basic demographic details were obtained and data collected regarding the patients' experience of LP, knowledge of the procedure, side effects/complications and expectations.

Complete data was obtained for 26 episodes (100% of cases). 69.2% of patients were female, mean age was 36.4 (range 19–61). 76.9% of the procedures were being performed to investigate a possible demyelinating disorder. For 88.5% this was their first LP.

Prior to LP levels of knowledge were mixed. 53.8% of patients correctly identified the site of needle insertion, 15.4% believed they would need a general anaesthetic and 7.7% thought the test was carried out in an operating theatre. 88.5% of patients were entirely happy with verbal information given in clinic about LP.

Post test 84.6% of patients were able to correctly identify the site of needle insertion. Type of anaesthesia and location of procedure were identified by all patients. There was a trend toward reduced satisfaction levels with information received from OPD; this was not significant ($p>0.05$).

These data suggest that a proportion of patients attending for day case LP did not fully understand the procedure prior to attendance. Though understanding improved post procedure satisfaction with information decreased.

048 THE NEUROLOGICAL EXAMINATION IN THE ACUTE MEDICAL ON-CALL

Y. Mohammed, O. Pirzada, S. Giles. *Nottingham City Hospital, Nottingham, UK*

Objectives: The neurological examination is part of the medical assessment that is conducted on all new medical admissions. The aim of the research was to assess if the neurological examinations were preformed on admissions and to address specific issues that junior doctors had when performing the examinations.
Methods: We conducted a retrospective case note review of all emergency admissions to general medicine over one week in a representative busy teaching hospital. This was followed by a questionnaire that was sent to the junior doctors inquiring about the structure of the admission's form; the doctors' confidence about the neurological examination; and any neurology teaching requirements.
Results: A total of 109 patients were reviewed. 56 patients (51%) did not have a neurological examination preformed or documented. The reason of the omission was stated in 9.3% of omissions only.

A total 39 doctors (15 pre-registration house officers and 24 senior house officers) completed the questionnaire. The major concern highlighted was the lack of neurological equipment available on the ward. Although the majority of doctors felt they were capable of conducting the examination, they still wanted more teaching.
Conclusion: Most medical admission will not include a neurological assessment of patients. Doctors' concerns about the examinations should be addressed to increase the number of assessments.

049 WHY DO CLINICIANS WHO TREAT NEUROLOGICAL DISEASE GET SUED?

A. McNeill. *Freeman Hospital & Royal Victoria Infirmary, Newcastle-upon-Tyne, UK*

Introduction: It would be helpful to know what the most common circumstances are that lead to litigation in neurological practice, but there are no studies of neurological negligence claims against NHS clinicians.
Methods: Summary data on negligence claims made against clinicians treating neurological disease from 1995–2005 was retrieved from the NHS Litigation Authority (NHSLA) database, which gathers data on all NHS negligence claims in England & Wales. For each case the specialty of the clinician, the primary pathology, the nature of the alleged misadventure and the severity of injury resulting from the misadventure was extracted. Data on 559 cases were available.
Results: The specialty most frequently cited was neurosurgery (241) followed by neurology (172). Non-neurologists and non-neurosurgeons were the defendant in 146 cases, predominantly general medicine (42), orthopaedic surgeons (39) and emergency physicians (33). The most common pathologies were intervertebral disc disease (27%), CNS tumours (21%), CNS infection (11%) and subarachnoid haemorrhage (9%). The most frequent misadventure was diagnostic error (44%), among non-neurologists (General Physicians and A&E doctors) this figure was significantly higher (59% Chi squared p = 0.049). In 47% of cases major permanent injury (eg blindness, hemiplegia) resulted from the misadventure. The patient died in 17% of cases, with non-neurologists having more fatalities (27% vs 17%, NS).
Discussion: For neurological negligence claims in the UK intervertebral disc disease is the most frequent pathology and diagnostic error the commonest misadventure. The high proportion of claims involving diagnostic error made by non-neurologists focuses attention on the need for specialist neurological assessment of patients.

050 ALTERED CHEMOSENSORY FUNCTION IN PARKINSON'S DISEASE

J. Deeb, M. Shah, L. J. Findley, C. H. Hawkes. *Essex Neuroscience Centre, Essex, UK*

Background: According to Braak staging of Idiopathic Parkinson's disease (IPD) the first lesions appear in the olfactory bulb and dorsal motor nuclei of IX and X. Although the adjacent solitary tract nucleus is relatively spared, it belongs to the salivary reflex pathway and may be compromised in early IPD.
Aim: To evaluate olfactory and taste function in patients with early IPD.
Methods: We tested 51 patients with early IPD (mean Hoehn & Yahr stage = 1.6), conforming to the UK-PD Brain Bank Diagnostic Criteria step 1 and scoring at least 27 on the Mini Mental Status Examination. Smell sense was evaluated with the University of Pennsylvania Smell Identification Test (UPSIT) and taste by the Rion TR-06 Electrogustometer. 46 healthy controls also underwent UPSIT and Electrogustometer tests.
Results: The mean UPSIT score was 32.9/40 for controls vs. 19.8/40 for IPD group ($p<0.001$). Taste threshold for the chorda tympani area was 11.06 dB for controls vs. 20.08 dB for IPD ($p<0.001$). For the Vallate Papillae area: 13.5 dB in controls vs. 19.9 dB in IPD ($p<0.001$).
Conclusion: Olfactory identification is markedly impaired in early Parkinson's disease. We also demonstrated for the first time that taste is abnormal in early IPD. Either test might be used diagnostically in the initial stages of disease. These changes may also explain why many patients with IPD display alteration in appetite and weight.

051 CHEMOSENSORY MEASUREMENT IN ESSENTIAL TREMOR

M. Shah, A. Noyce, J. Deeb, L. J. Findley, C. H. Hawkes. *Essex Neuroscience Centre, Romford*

Objective: Tremulous Parkinson's disease may be confused with essential tremor. Smell and taste are abnormal in early stage Parkinson's disease but probably not at any stage in essential tremor. We wished to determine whether chemosensory testing is normal in essential tremor and if so this might help distinguish it from Parkinson's disease.
Methods: Three procedures were used: (1) University of Pennsylvania Smell Identification test (UPSIT); (2) Smell Threshold Test (Sensonics Inc) using phenylethylalcohol in (i) 45 healthy controls, mean age 49 years (range 17–93), (ii) 50 essential tremor patients mean age 62 years (range17–82); (3) taste threshold measurement with Rion TR-06 electrogustometer applied to (i) tip of tongue (chorda tympani; CT), (ii) base of tongue over the most lateral vallate papilla (VP; IX). All participants scored at least 27/30 on the Mini-Mental Status Test.
Results: There were no significant differences in any control v essential tremor comparisons as follows (t test, $p>0.05$): (1) Mean UPSIT scores between controls and essential tremor (32.8/40 v 32.3/40; (2) mean control smell thresholds: −6.7vol/vol compared to −6.3vol/vol for essential tremor; (3) Mean taste threshold: controls CT: 11.2dB; VP: 13.5dB. essential tremor CT: 13.5dB and VP 14.6dB.
Conclusions: Smell sense and taste threshold are normal in essential tremor compared to healthy controls. This information may be of value in distinguishing essential tremor from tremulous Parkinson's disease patients.

052 IDENTIFICATION OF LRRK2 MUTATIONS IN PARKINSON'S DISEASE

A. J. Lewthwaite, D. J. Nicholl, K. E. Morrison. *University of Birmingham, University Hospital Birmingham, Sandwell & West Birmingham Hospitals, Birmingham, UK*

Background: Parkinson's disease is the second most common neurodegenerative disease after Alzheimer's disease. Recently mutations in the PARK8 gene leucine rich repeat kinase 2 (LRRK2) have been identified. Indeed a single LRRK2 mutation G2019S appears to account for up to 5–6% of familial and 1–2% of sporadic Parkinson's disease cases. LRRK2 PD has age of onset, clinical features and treatment response typical of sporadic Parkinson's disease, with highly variable neuropathology.
Aims and Methods: To assess G2019S LRRK2 mutation frequency in predominantly sporadic Parkinson's disease samples and controls using a restriction digest technique with SfcI enzyme.
Results: In 110 Parkinson's disease samples screened so far we have identified 1 patient who is a heterozygote for G2019S mutation. The base substitution was confirmed by sequencing. No G2019S mutations were observed in 30 controls. The clinical features of this patient appear typical of sporadic Parkinson's disease.
Conclusions: We have demonstrated a G2019S mutation frequency of 0.9% in our sample of predominantly sporadic Parkinson's disease patients which concurs with figures previously reported. The phenotype of this patient appears typical of sporadic Parkinson's disease. We plan to screen for this mutation in more sporadic Parkinson's disease samples, controls and familial Parkinson's disease samples as part of a more extensive ongoing study of LRRK2 related Parkinsonism.

053 SYSTEMATIC REVIEW OF THE PREVALENCE OF DEPRESSION IN PARKINSON'S DISEASE

C. Counsell, K. Taylor, M. Appukutty. *Department of Medicine & Therapeutics, University of Aberdeen, Aberdeen, Scotland*

Background: Depression is common in people with Parkinson's disease and is a major determinant of their quality of life. However, the reported prevalence rates vary widely. We systematically reviewed the literature to identify factors associated with this variation.
Methods: Articles that reported the prevalence of depression in Parkinson's disease were located using several search strategies. The study methods were summarised and the results stratified by methodological factors and patient characteristics.
Results: Fifty studies were included. There was enormous variation in the prevalence of any depression and severe depression in Parkinson's disease, which was not fully explained by study or patient characteristics. Using the most rigorous criteria, the median prevalence of any depression and severe depression was approximately 30% and 20% respectively. Reduced cognitive function and higher levels of disability were consistently associated with higher rates of depression. Depression was more prevalent in women with Parkinson's disease than men (OR 2.98, 95% CI 2.39 to 3.71), and in Parkinson's disease patients than healthy controls (OR 5.70, 95% CI 4.38, 7.42) and controls with other chronic diseases (OR 2.51, 95% CI 1.89 to 3.33).
Conclusions: Depression is a major problem in Parkinson's disease but the variation in prevalence is poorly explained. Future studies should standardise their methods to allow meta-analysis.

054 THE USE AND INFLUENCE OF FP-CIT SPECT IN CURRENT PRACTICE. UK EXPERIENCE OF 190 PATIENTS WITH UNCERTAIN PARKINSONISM

V. L. Marshall, J. Patterson, D. Hadley, K. Grosset, D. Grosset, on behalf of the UK FP-CIT Study Group. *Departments of Neurology, Clinical Physics & Neuroradiology, Institute of Neurosciences, Southern General Hospital, London, UK*

Background: The clinical diagnosis of parkinsonism and its causes remains imperfect. Brain dopamine transporter imaging (eg FP-CIT SPECT) is useful in uncertain cases because it demonstrates loss of dopaminergic neurons in degenerative parkinsonism (eg Parkinson's disease) but is normal in non-degenerative conditions (eg essential tremor; drug-induced/vascular/psychogenic parkinsonism).
Aim: To observe the current practice of FP-CIT SPECT in patients with uncertain parkinsonism (ie diagnosis of degenerative parkinsonism versus non-degenerative parkinsonism/essential tremor was uncertain).
Methods & Results: 190 patients with uncertain parkinsonism underwent FP-CIT imaging in 8 centres. Clinical features and diagnosis were registered centrally before and after knowledge of scan result. FP-CIT clearly confirmed or excluded a pre-synaptic deficit in 184/190 (97%) as follows: clearly abnormal in a parkinsonian pattern (n = 82), a focal pattern suggestive of vascular disease (n = 4) or clearly normal (n = 98). This was consistent with the pre-scan clinical diagnosis in 135/184 (73%). Congruence between the clinician's diagnosis and scan improved after the scan result to 179/184 (97%). The scan was abnormal in a non-parkinsonian pattern or borderline in 6/190 (3%), in whom the clinical diagnosis remained uncertain post-scan in 3 (50%).
Conclusion: FP-CIT SPECT clearly categorises most patients with clinically uncertain parkinsonism. The scan result differs from the pre-scan diagnosis in one quarter but is usually consistent with the post-scan diagnosis.

055 YOUNG ONSET, ATYPICAL PROGRESSIVE SUPRANUCLEAR PALSY IN A PATIENT CARRYING THE TAU EXON 10 +16 MUTATION

J. M. Partridge, P. Heutink, M. P. Carey, R. N. Corston, D. J. Nicholl. *Neurology Department, Queen Elizabeth Hospital, University Hospital of Birmingham NHS Trust, Birmingham, UK*

Objective: To describe the clinical course, neuropathology and detection of the tau exon 10 +16 mutation in a patient with a young onset and unusual presentation of progressive supranuclear palsy (PSP).
Case report: A previously healthy 41-year-old man with an akinetic-rigid syndrome initially presented with bradykinesia, pyramidal signs, depression and bilateral vocal cord paralysis that progressed over 10 months with ensuing respiratory failure. He displayed no early falls, gaze palsy or significant levodopa response. There was a family history of early onset dementia.
Results: Investigation for multisystem extrapyramidal, metabolic and familial conditions proved unhelpful. Neuropathological examination at post mortem demonstrated changes of PSP consisting of tau positive neurofibrillary tangles, neuropil threads and glial inclusions with tufted astrocytes and coiled bodies, though unusually there was prominent cerebral cortical involvement without dentate nucleus pathology. Sequencing of his tau gene showed the exon 10 +16 mutation associated with fronto-temporal dementia with parkinsonism-17.
Conclusions: This case emphasizes the importance of considering a hereditary tauopathy in a patient presenting with a young onset rapidly progressive akinetic-rigid disorder with a possibly significant family history, even in the absence of the typical clinical features of PSP.

056 AN EPIDEMIOLOGICAL STUDY OF MULTIPLE SCLEROSIS IN THE NORTH EAST OF NORTHERN IRELAND

O. M. Gray, G. V. McDonnell, S. A. Hawkins. *Queens University, Belfast, Northern Ireland; Royal Victoria Hospital, Belfast, Northern Ireland*

Objective: To estimate the prevalence of multiple sclerosis.
Background: NI has been recognised to be an area of high risk for multiple sclerosis. The original study of Allison and Millar in 1951 found a prevalence of 41 per 100 000. Subsequent studies in 1951, 1961, 1986 and 1996 suggested prevalence rising serially −57, 104 and 168.2 per 100 000.
Methods: We surveyed the North East of Northern Ireland (population 160 400, area 2030 km^2). Sources of cases included the Northern Ireland Neurology Service records, general practitioners, hospital discharge coding, multiple sclerosis charities, multiple sclerosis specialist nurses and respite facilities. Cases complied with the Poser criteria or the McDonald criteria.
Results: From a provisional list of 469 cases, 370 (123 males, 247 females) were identified with definite multiple sclerosis. The prevalence was 230.7 per 100 000 with a significantly higher prevalence in females (370.8/100 000) than males (195.7/100,000). Mean age on prevalence day was 50.3 years (SD 14.0). Mean age at onset was 32.6 years (SD 10.5). Mean delay between onset and diagnosis was 4.6 years.
Conclusions: Northern Ireland continues to have a rising prevalence of multiple sclerosis. This may in part be due to improved case ascertainment, improved diagnostic techniques and improved awareness of multiple sclerosis.

057 ELEVATED URINARY EXCRETION OF ALUMINIUM AND IRON IN MULTIPLE SCLEROSIS

G. Mamutse, C. Exley, O. Korchazhkina, E. Pye, S. Strekopytov, A. Polwart, C. P. Hawkins. *Keele Multiple Sclerosis Research Group; Birchall Centre for Inorganic Chemistry and Materials Science; Institute for Science and Technology in Medicine; Life Sciences (Keele University, UK)*

Background: Iron is deposited in the brain in multiple sclerosis and may contribute to the pathogenesis of the disease by promoting oxidative stress which may cause selective oligodendrocyte cell death with consequent demyelination. Oxidative stress may also directly damage myelin through lipid peroxidation producing malondialdehyde (MDA). Aluminium- a pro-oxidant- could, if present, potentiate iron-induced oxidative damage.
Methods: We used battery of analytical techniques to determine the urinary excretion of (i) markers of oxidative damage- MDA and thiobarbituric acid reactive substances (TBARS), (ii) iron and the environmental toxin aluminium and its antagonist, silicon in 10 subjects with relapsing-remitting multiple sclerosis (RRMS), 10 with secondary progressive multiple sclerosis (SPMS) and in a comparative group of 10 age- and sex-matched healthy volunteers.
Results: Urinary concentrations of MDA and TBARS were similar among the three groups. Relative to the control group, urinary concentrations of iron were significantly increased in the SPMS group ($p<0.01$) while those of aluminium were significantly increased in both the RRMS ($p<0.001$) and SPMS ($p<0.05$) groups. Silicon excretion was significantly reduced in the SPMS group ($p<0.05$).
Conclusion: We demonstrate increased urinary excretion of aluminium and iron in multiple sclerosis. Further studies to confirm and elucidate these findings are planned.

058 INEQUALITIES IN THE PROVISIONS OF DISEASE MODIFYING THERAPIES FOR MULTIPLE SCLEROSIS IN THE UK

N. Evangelou, A. Karsay, T. Owens. *Dept of neurology Queen's medical centre and Department of Economics, University of Nottingham, Nottingham, UK*

Access to disease modifying therapies (DMTs) for multiple sclerosis in the UK had been the subject of national debate. Geographical variations in the use of expensive medications has been referred to by the media as the ''postcode lottery of prescribing''. While the Risk Sharing Scheme of the Department of Health has facilitated wider prescribing of DMTs, it is unclear whether it has affected individual inequalities in access to healthcare.

This research measures individual level inequalities by examining whether the chance of receiving DMTs is related to a patient's level of socio-economic status. Using data for 2538 patients with multiple sclerosis, of which 521 received treatment, we examine DMT prescribing rates in 2 UK centres. In addition to clinical parameters we include the level of socio-economic deprivation of the individual. We find that patients lower in the socio-economic ladder are less likely to be receiving DMTs. This holds true regardless of the deprivation index used (Index of Multiple Deprivation, Carstairs and Townsend). As the patients deprivation score increases by one unit, the odds of receiving treatment falls by 1.7%.

059 LONGITUDINAL STUDY OF CHEMOKINE RECEPTOR EXPRESSION ON CD4+ AND CD8+ T CELLS AND CD14+ MONOCYTES IN PATIENTS WITH RELAPSING AND REMITTING MULTIPLE SCLEROSIS

O. Suliman, S. J. Howell, J. Lawry, B. Sharrack, M. N. Woodroofe. *Biomedical Research Centre, Sheffield Hallam University, Sheffield, UK; Royal Hallamshire Hospital, Glossop Road, Sheffield, UK; BD Biosciences, 21 Between Towns Road, Cowle, Oxford, UK*

Chemokines are chemoattractant cytokines which are involved in the directional migration of cells from the blood into the CNS in the pathogenesis of multiple sclerosis. Two chemokines, CCL2 and CXCL10, which bind to their corresponding receptors CCR2 and CXCR3 on peripheral blood mononuclear cells, have been identified in the CNS in multiple sclerosis at inflammatory foci. We have undertaken a 12 month longitudinal study of 30 patients with relapsing remitting multiple sclerosis and 10 healthy volunteers and bimonthly we have assessed expression of CCR2 and CXCR3 on peripheral blood T cells and monocytes, using three colour flow cytometry. Preliminary results have shown that 17 of the multiple sclerosis patient group had relapses during this 12 month period. CXCR3 was consistently expressed by 38% of the multiple sclerosis and 44.3% of control group whereas very low numbers of T cells expressed CCR2 (3.5% by patients and 3.1% by controls). Conversely monocytes were strongly positive for CCR2 (patients 80.9%, controls 82.6%) and low percentages of CXCR3+ cells were detected ($<$6% for both groups). Preliminary results suggest that no significant changes in receptor expression were associated with relapses. These results are in contrast to previous studies which demonstrated increased CXCR3 expression at times of relapse.

060 NEURODEGENERATION IN A MARMOSET MODEL OF MULTIPLE SCLEROSIS

I. M. Pomeroy, E. K. Jordan, J. Frank, P. M. Matthews, M. M. Esiri. *Dept. of Clinical Neurology, University of Oxford, Oxford, UK; Laboratory of Diagnostic Radiology Research, National Institutes of Health, USA*

Introduction: Neurodegenerative features such as cerebral atrophy are increasingly recognised in multiple sclerosis and have been shown to be correlated with disease progression. In this study we have set out to look for evidence of neurodegenerative features in an animal model of multiple sclerosis.
Methods: We examined the brains of marmosets with EAE and control animals using immunohistochemical markers to study neurones, oligodendrocytes, astrocytes and cortical thickness. We used quantitative techniques to compare findings in cortical lesions, normal appearing grey matter (NAGM) and control brains.
Results: There was a 20% loss of neurones within leucocortical lesions in the deep layers of the cortex but no significant change in superficial subpial lesions. Neuronal size was decreased in both leucocortical (16%) and subpial lesions (18%) as well as in the NAGM of deep cortical layers (14%). Oligodendrocytes were increased in size and decreased in density in both types of cortical lesion. Cortical thickness was decreased in areas containing cortical lesions (17%) and in areas of NAGM (20%).
Discussion: This study provides evidence for substantive neurodegenerative changes occurring within cortical lesions and NAGM of this animal model and suggests that marmoset EAE may be a useful model for studying the interaction between neurodegenerative and inflammatory processes in multiple sclerosis.

061 STIMULATION OF TOLL-LIKE RECEPTOR 3 (TLR3) SUPPRESSES AN ANIMAL MODEL OF MULTIPLE SCLEROSIS BY INDUCING ENDOGENOUS INTERFERON BETA

T. Touil, D. Fitzgerald, A. Rostami, B. Gran. *Department of Neurology, Thomas Jefferson University, Philadelphia, USA; Division of Clinical Neurology, University of Nottingham, Nottingham, UK*

Interferon beta (IFNb) is given by injection as the most common immunomodulatory treatment for multiple sclerosis. Microbial components can induce the production of endogenous IFNb by antigen-presenting cells through stimulation of Toll-like receptor (TLRs), key components of the innate immune system.

We tested the hypothesis that polyinosinic-polycytidylic acid (poly I:C), a TLR3 agonist and potent type I interferon inducer, can modulate inflammatory demyelination in experimental autoimmune encephalomyelitis (EAE), an animal model of multiple sclerosis.

Female SJL mice were immunized with a proteolipid protein (PLP) peptide and received intraperitoneal (i.p.) poly I:C or PBS during the induction or the relapsing phase of disease. Clinical, pathological, and immunological parameters were assessed.

Treatment with poly I:C suppressed clinical and pathological signs of EAE. Poly I:C treatment induced increased expression of IFNb in the spleens of treated mice. Spleen cells from poly I:C-treated mice cultured in the presence of the PLP peptide produced increased levels of the CC-chemokine CCL2. Neutralization of either IFNb or MCP-1 in vivo by injection of neutralizing antibodies reversed disease suppression by poly I:C. In vitro neutralization studies showed that the production of MCP-1 was IFNb-dependent.

We conclude that poly I:C treatment suppresses EAE by mechanisms that involve IFNb and CCL-2.

062 SUBJECTIVE AND OBJECTIVE TREMOR MEASUREMENT IN PATIENTS WITH MULTIPLE SCLEROSIS

A. N. Merriman, C. L. Hirst, E. Mason, R. W. Marshall, T. P. Pickersgill, N. P. Robertson. *Department of Neurology, University Hospital of Wales, Cardiff, Wales; Department of Pharmacology, University Hospital of Wales, Cardiff, Wales*

Sequential patients with multiple sclerosis attending a regional clinic were invited to participate in the study. Patients were assessed according to a standardised protocol employing a tremor specific activities of daily living questionnaire, subjective tremor score (0–10) and multiple sclerosis disability score (EDSS).Objective analysis of tremor used an Entran EGAX-5-/R(3 dimensional) accelerometer transducer attached to the third digit and the Cardiff tremor acquisition and analysis system.Subjects were asked to extend the distal upper limb in a standardised pattern and information acquired over 4$\times$10 sec epochs compared to normative data.

99 patients were recruited (21 males:74 females) mean age 41 years and EDSS 4.3. 56% patients reported significant tremor with a mean subjective score of 2.9 (range 1–8) and mean ADL score 39.5 (range 25–88), although objective evidence of abnormal tremor was measured in only 25% (mean freq 6.6, mean peak power 997 mg). Correlations were identified between subjective score and total power (mg) $r = 0.332$ ($p = 0.001$), ADL score and total power $r = 0.265$ ($p = 0.008$), objective score and ADL score $r = 0.4$ ($p<0.001$).

Poor correlation between ADL score, subjective score and total power suggests that the tremor ADL scale may not be specific in patients with multiple sclerosis and other factors may contribute to impairment. Patients are poor at judging whether they have abnormal tremor which is best analysed objectively prior to therapeutic intervention.

063 TOWARDS DEFINING ANTIGENIC TARGETS FOR ANTIBODIES IN MULTIPLE SCLEROSIS

E. T. Littleton, M. Dreger, J. Palace, A. Vincent. *Neurosciences Group, Weatherall Institute of Molecular Medicine, John Radcliffe Hospital, Oxford, UK; Department of Physiology, University of Oxford, Oxford, UK; Department of Clinical Neurology, Radcliffe Infirmary, Oxford, UK*

Autoantibodies are thought to play some roles in the pathogenesis of multiple sclerosis but past research has failed to identify, consistently, relevant disease-associated antigens. We used a range of techniques to

look for antibodies to central nervous system antigens in 100 multiple sclerosis patients, comparing with a group of 20 healthy and other controls. Conventional immunohistochemical and western blotting methods, that are known to be most suitable for identifying intracellular antigens (for instance, those serving as diagnostic markers of paraneoplastic diseases), did not clearly distinguish multiple sclerosis patient sera from control sera: there were no characteristic multiple sclerosis -associated immunohistochemical staining patterns on rat cerebellar sections, and no characteristic patterns of bands on western blots of rat brain extracts or neuronal or oligodendroglial cell extracts. We concentrated instead on techniques suitable for identifying cell surface antigens. By immunofluorescence, the sera of about 10% of multiple sclerosis patients contained IgG which bound to the surface of unpermeabilised neuronal or oligodendroglial cell lines. A few of these positive sera specifically immunoprecipitated antigens at 20 kDa and 30 kDa from neuronal or oligodendroglial cell extracts. Following further purification and separation of the immunoprecipitates, we are identifying the antigens by mass spectrometry.

064 ALTERED CORTICAL ACTIVATION IN AMYOTROPHIC LATERAL SCLEROSIS (ALS) DIFFERS IN MOTOR AND EXTRA-MOTOR REGIONS

B. R. Stanton, V. C. Williams, P. N. Leigh, C. Blain, A. Simmons. *Institute of Psychiatry, King's College London, London, UK*

We tested the hypothesis that patients with ALS show increased cortical activation during a motor task when compared to healthy controls and to patients with muscle weakness due to lower motor neurone (LMN) syndromes.

fMRI was used to measure activation during a block design paradigm contrasting freely selected right hand movements against rest in 16 patients with ALS, nine patients with LMN disorders (matched for upper limb weakness) and seventeen healthy controls.

During the motor task, patients with ALS showed increased cortical activation bilaterally, extending from the sensorimotor cortex (areas 1, 2, 4) into the inferior parietal lobule (area 40) and the superior temporal gyrus (area 22) when compared to LMN patients and controls. In addition, ALS patients showed reduced activation in pre-frontal regions (areas 8, 9, 10, 32).

Our results show that increased activation in motor areas and reduced activation in pre-frontal regions previously described in ALS subjects can be demonstrated through a single paradigm. Importantly, we have shown that these changes are not simply an artefact of weakness or task difficulty, but relate specifically to upper motor neurone pathology in ALS. ALS may provide a useful model to explore the mechanism of cortical adaptation in neurodegenerative disorders.

065 A NEW SYNDROME OF CONGENITAL INSENSITIVITY TO PAIN DIAGNOSED BY SKIN BIOPSY AND CONTACT HEAT EVOKED POTENTIALS (CHEPS)

P. Facer, D. Atherton, K. Roberts, V. P. Misra, M. Kinali, A. Y. Manzur, F. Muntoni, P. Anand. *Peripheral Neuropathy Unit, Division of Neuroscience and Mental Health, Imperial College London, UK, Hammersmith Hospital, London, UK*

Congenital insensitivity to pain can be difficult to diagnose in young children, and is usually associated with loss of skin flare responses and mutations in the nerve growth factor (NGF) signalling pathway. We present an infant (14 months old female) with a history of painless injuries, and selective absence of behavioural responses to noxious thermal and mechanical stimuli, but with a normal histamine-induced skin flare. A second infant (5-year-old male) has been followed up over 3 years with similar findings, although thermal and mechanical stimuli were recently distinguished as noxious. Both children had absent cerebral heat evoked potential responses, in contrast to clinically unaffected siblings. Skin biopsies from both infants showed severely reduced or absent intra-epidermal fibres immunoreactive for capsaicin receptor (TRPV1 mean fibres/mm length of epidermis: 14 months female = 2.5 and 5 years old male = 0.0; control skin = 40.0) and PGP9.5, a nerve marker. However, remarkably, sub-epidermal nerve fibres were similar to controls for a range of markers including the NGF-regulated neuropeptides CGRP and substance P, which may account for the preserved skin flares. We hypothesize that these patients may lack or have delayed spinal cord connectivity of nociceptor fibres, and a better prognosis.

066 MNGIE NEUROPATHY MIMICKING GUILLAIN-BARRÉ SYNDROME

L. Ginsberg, J-W. Taanman. *University Department of Clinical Neurosciences, Hampstead Campus, Royal Free and University College Medical School, University College London, London, UK*

Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) is an autosomal recessive disease caused by mutations in the gene for thymidine phosphorylase. Clinically, peripheral neuropathy is prominent, along with gastrointestinal dysmotility, asymptomatic white matter lesions and mitochondrial myopathy. We report a patient with MNGIE in whom the abrupt onset of neuropathy led to diagnostic confusion with Guillain-Barré syndrome (GBS). The patient presented at age 12 with lower limb weakness, areflexia and sensory symptoms, reaching a nadir within 3 weeks. There were electrical features of a demyelinating neuropathy. A presumptive diagnosis of GBS was made. There was partial improvement over the next 6 months. Six years later, her weakness worsened. The presence of ophthalmoplegia, gastrointestinal symptoms, cerebral white matter lesions on MRI, and lactic acidosis led to a diagnosis of MNGIE. This was confirmed by finding elevated plasma thymidine and deoxyuridine levels. DNA sequencing showed compound heterozygous thymidine phosphorylase gene mutations (point mutation at the splice junction of intron 2 and 6-base pair deletion in exon 9). The splice junction mutation leads to skipping of exons 2 and 3; the nucleotide deletion is predicted to cause deletion of amino acids Leu397 and Ala398. Patients with MNGIE may therefore present with an acute neuropathy resembling GBS.

067 NEPHROTIC SYNDROME IN GUILLAIN-BARRÉ SYNDROME

T. P. Harrower, M. Clatworthy, N. Pritchard, J. Brown, G. G. Lennox, M. Griffiths, S. Thiru, D. Menon. *Department of Neuroscience, Department of Nephrology, Department of Pathology, Department of Anaesthetics, University of Cambridge, Addenbrooke's Hospital, Cambridge, UK*

Guillain-Barré Syndrome (GBS) is an acute immunological disorder, which classically produces weakness, sensory deficits areflexia and autonomic dysfunction, which can be caused by prior infection or immunisation for influenza. We describe two cases with severe GBS occurring two months after influenzae vaccination. Both cases were treated with intravenous immunoglobulin (IVIg) and both cases developed severe nephrotic syndrome without significant nephritis or overt renal failure. Renal biopsy in both cases showed minimal change Glomerular-nephritis with minimal immunoglobulin deposition with no features compatible with the more commonly described hyperosmotic oedematous acute tubular necrosis, which can occur in conjunction with IVIg administration. Both cases had full recovery of renal function although one case required high dose steroids.

The two patients received different formulations of influenzae vaccinations (live attenuated and dead protein antigen), and they received immunoglobulins produced by different manufacturers, thus suggesting that contamination of a batch of immunoglobulin unlikely.

It is more likely that the nephrotic syndrome has arisen as the nephrons are also targeted by the immune process which is producing the peripheral nerve damage and therefore nephrotic syndrome should be considered as a potential complication of GBS.

068 OCULAR FIXATION IS ABNORMAL IN MOTOR NEURONE DISEASE

C. Donaghy, R. Pinnock, V. Patterson, C. McGivern, M. Gibson. *Department of Neurology, Royal Hospitals Trust, Belfast, Northern Ireland; Regional Medical Physics Department, Royal Hospitals Trust, Belfast, Northern Ireland*

Background: Although typical pathology has been identified in ocular motor nuclei of motor neurone disease (MND) patients, studies have described abnormalities of saccadic eye movements, felt to be consistent with prefrontal cortical dysfunction. Fixation however has not been formally examined in MND and functional imaging has not implicated the frontal cortex.
Objectives: To examine for abnormalities of fixation in patients with MND.
Methods: Eye movements with and without a target were recorded in 19 MND patients and 23 age-similar controls using an infra-red Scalar limbus system. Geometric mean saccadic intrusion amplitudes (GMSIA) and geometric mean fixation periods (GMFP) were calculated with and without a target. All patients received the Amyotrophic Lateral Sclerosis Functional Rating Scale revised (ALS-FRSr) and a neuropsychological battery.

Results: GMSIA (target on) was significantly larger in the MND group as compared to controls ($p = 0.045$) and the bulbar onset MND patients when compared to controls ($p = 0.019$). A significant correlation was found between GM SIA (target on) and ALS FRSr score ($p<0.05$) in patients but no correlation was found with tests of frontal lobe function.
Conclusions: Ocular fixation is abnormal in MND particularly of bulbar onset. These abnormalities of ocular fixation may be accounted for by brainstem dysfunction.

069 PARANEOPLASTIC CIDP ASSOCIATED WITH TRANSITIONAL CELL CARCINOMA: A CASE REPORT AND REVIEW OF THE LITERATURE

R. Patani, M. P. Lunn, M. Groves, M. M. Reilly. *Centre for Neuromuscular Disease, National Hospital for Neurology and Neurosurgery, Queen Square, London, UK*

Paraneoplastic neurological syndromes are a heterogeneous group of non-metastatic manifestations of malignancy. They are believed to be immunologically mediated. The classical paraneoplastic syndrome affecting peripheral nerves is sub-acute sensory neuronopathy. Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) as a paraneoplastic phenomenon is only rarely encountered outside of the association with plasma cell dyscrasia.

We present a 76-year-old female with an IgG-associated CIDP who became treatment resistant after three years of stability. An occult transitional cell carcinoma of the bladder (G2pT1b) was revealed after extensive investigation. Following intra-vesical treatment for the malignancy her CIDP came under control. Three subsequent objective deteriorations heralded a recurrence of the tumour. Response to intravenous immunoglobulin was returned with tumour treatment on each occasion. No antibodies have been identified to explain the mechanism of disease deterioration.

This is the first described case of paraneoplastic CIDP associated with a transitional cell carcinoma of the bladder. CIDP may behave as a paraneoplastic disease. A thorough search for malignancy should be undertaken when response to treatment is lost in CIDP.

070 PATIENTS WITH HMSN-1 PRESENTING WITH TYPICAL HNPP PHENOTYPE

A. Al Saleh, A. Oware. *Department of Clinical Neurophysiology, Frenchay Hospital, Bristol, UK; Department of Clinical Neurophysiology, Gloucestershire Royal Hospital, Gloucester, UK*

Hereditary Motor and Sensory Neuropathy type 1 (HMSN-1) is the most common of the inherited polyneuropathies. Nerve conduction study is essential in establishing the diagnosis. It is standard practice that motor nerve conduction study should show uniform slowing below 75% of the lower limits of normal in all nerves of patients with HMSN-1. Conduction velocity of 38 metre per second is considered the cut-off value in most labs.

We report two patients in whom motor nerve conduction studies showed conduction velocities more than 45 m/s in some nerves, with other features of demyelinating neuropathy affecting mainly the pressure points which was very suggestive of Hereditary Neuropathy with liability to Pressure Palsy (HNPP) and these were not typical of HMSN-1. Genetic testing confirmed that one of the patients had 17p11.2 duplication in PMP22 gene and the other patient had PMP22 mutation both are diagnostic of HMSN-1. Neither patient had PMP22 deletion as expected in HNPP.

We believe that the electrophysiological diagnostic criteria for hereditary neuropathies should be reviewed taking into consideration the advances in molecular genetics.

071 SPONTANEOUSLY RESOLVING PARANEOPLASTIC OCULAR FLUTTER-OPSOCLONUS-MYOCLONUS SYNDROME IN ASSOCIATION WITH TREATMENT-SENSITIVE LAMBERT-EATON MYASTHENIC SYNDROME

R. J. Simister, K. Ng, M. Beckles, D. Chao, B. Lang, D. J. H. McCabe. *University Dept of Clinical Neurosciences, Dept of Oncology, and Dept of Respiratory Medicine, Royal Free and University College Medical School, Royal Free Hospital, London, UK; Neurosciences Group, Weatherall Institute of Molecular Medicine, Oxford, UK*

Background: A paraneoplastic cerebellar syndrome may occur in association with Lambert-Eaton myasthenic syndrome (LEMS), but the co-occurrence of paraneoplastic ocular flutter-opsoclonus-myoclonus syndrome and LEMS has not been previously reported. Spontaneous resolution of paraneoplastic ocular flutter-opsoclonus-myoclonus syndrome has not been described.
Case Report: A 67-year-old woman developed complex partial seizures, increasing ocular flutter, opsoclonus, myoclonus, and cerebellar signs, which improved spontaneously six weeks after symptom onset and before initiation of any immuno-modulatory or anti-neoplastic therapy. Approximately eight weeks after symptom onset, the patient became encephalopathic, she had a further complex partial seizure, and she became areflexic with potentiation of deep tendon reflexes following repetitive exercise. Radiological, endoscopic and histological investigations revealed a small cell lung cancer. Neurophysiological investigations at the time of development of limb areflexia confirmed a diagnosis of LEMS, and high titre anti-voltage gated P/Q-type calcium channel antibodies were identified in the serum. The encephalopathy and clinical features of LEMS responded dramatically to chemotherapy and radiotherapy.
Conclusions: Spontaneous remission of paraneoplastic opsoclonus-myoclonus syndrome may occur, and this syndrome may occur in association with LEMS.

072 A RARE CAUSE OF FATAL INTRACRANIAL HAEMORRHAGE

A. Neligan, G. Mullins, H. L. Chua, P. Fitzgerald, B. J. Sweeney, H. Harrington. *Department of Neurology, Mercy University Hospital, Ireland*

We report the case of a 53-year-old farmer with a 5 day history of severe headaches, photophobia and neck stiffness. Past medical history was non-contributory. Physical exam was normal apart from neck stiffness. Full blood count (platelets 173), coagulation screen were normal throughout. Liver function tests remained normal apart from an elevated gamma-GT (156) CT Brain was normal. CSF analysis showed a WCC of 454/cmm (60% lymphocytes), elevated CSF protein (1.42 g/l) and a normal CSF glucose. He was commenced on IV antibiotics and IIV acyclivor and improved. On day 3 of admission, he complained of a sudden severe headache, became unresponsive (GCS 3/15) and was intubated. Repeat CT brain showed a massive left parenchymal and intraventricular haemorrhage. He died 4 days later.

Subsequent serum serology for leptospirosis was positive with an IgM titre of 1:640. A repeat sample taken 4 days post admission showed a raising IgM titre of 1:1280 indicating active leptospirosis. Detailed pathological examination confirmed intracerebral haemorrhage with normal cerebral vasculature.

Leptospirosis is a rare cause of intracerebral haemorrhage even there is no evidence of coagulopathy and has been described in only a handful of cases.

073 CAROTID DISSECTION PRESENTING AS EVOLVING NEUROLOGIC SYMPTOMS OVER A SPAN OF WEEKS TO MONTHS- TWO CASE REPORTS

R. J. Abraham, C. Sherrington, J. Sussman. *Centre for Clinical Neurosciences, Hope hospital, Manchester, UK*

Background: Spontaneous cervical artery dissection is an important cause of stoke in young adults (about 20%). Most of the cerebral infarcts occur within the fist week of the initial symptom. Late presentations are very rare.
Case report: Mr M is a 39-year-old man with hypertension and smoker presented with progressive pyramidal weakness of left leg over a period of four months. Magnetic resonance scan and MRA showed multiple areas of infarcts (magnetic resonance picture is not typical of stroke) in the right MCA territory with evidence of carotid dissection.
Case 2: This 34-year-old lady, smoker, ex-alcoholic presented with a 5 weeks history of stepwise neurological symptoms (mainly sensory) of the right side of the body. These events happened in a step wise manner over a span of 4 to 5 weeks before presentation. Magnetic resonance and MRA were similar to the above case.
Conclusion: Here we have two cases of carotid dissection with rare but similar presentation. Both of them had weeks and months history of progressive neurological symptoms, presumably embolic, before the presentation. The above may represent a subgroup of patients with carotid dissection who may have recurrent/progressive symptoms for many weeks to months before presentation.

074 HAEMOSTATIC DRUGS: THE NEW HOPE FOR PRIMARY INTRACEREBRAL HAEMORRHAGE

R. Al-Shahi, Y. Hong. *Division of Clinical Neurosciences, Centre for Clinical Brain Sciences, University of Edinburgh, Scotland*

Background: Primary intracerebral haemorrhage (PICH) accounts for 615% of all strokes, and 38% survive the first year. Because PICH volume influences its outcome and a third of PICHs enlarge by a third within 24 hours of onset, early haemostatic drug therapy might improve outcome.
Methods: In August 2005, we sought randomised controlled trials (RCTs) of haemostatic drugs for PICH in Ovid Medline and Embase, the Stroke Trials Directory, the Cochrane Stroke Group Trials Register, and in the bibliographies of relevant articles. Two reviewers extracted data and sought missing data from RCT corresponding authors. Meta-analysis was performed with Review Manager 4.2.7.
Results: We found 1 phase II RCT of aminocaproic acid (3 participants) and 3 phase II RCTs of recombinant activated factor VII (rFVIIa) (486 participants). Every RCT had methodological faults. Although treatment caused a non-significant increase in thromboembolic adverse events, overall it improved secondary clinical outcomes at day 90, such as death (risk reduction (RR) 33%, 95% CI 3% to 54%), and dependence defined as scores 4–6 on the modified Rankin Scale (RR 22%, 95% CI 8% to 33%).
Conclusions: An ongoing phase III RCT may confirm that rFVIIa is a clinically effective treatment for PICH, but less expensive drugs may be effective and merit RCTs.

075 HOW OFTEN DO PATIENTS DRIVE TO A TIA CLINIC?

M. O. McCarron, M. P. McNicholl. *Department of Neurology, Altnagelvin Hospital, Londonderry, Northern Ireland*

In the UK certain medical standards have to be attained for an individual to hold a driving licence. After a single transient ischaemic attack (TIA) or minor stroke the Driving and Vehicle Licensing Authority (DVLA) recommends a group 1 driving restriction for one month. We sought to determine how often the DVLA guidelines were applied following a TIA or minor stroke prior to attending a TIA clinic.

Patients were recruited prospectively at a TIA clinic over a three month period. Age, sex, diagnosis and frequency of previous driving, recall of driving advice from referring doctor and whether the patient had driven to the clinic were recorded.

Forty eight new patients (24 men, mean age 57.7 $\pm$ SD 14.9 years) were studied. Twenty-six (54%) were previous drivers. Fifteen (31%) drove to the clinic. Seven (15%) recalled driving advice from their referring doctor. Among 22 patients (46%) with a confirmed diagnosis of TIA or stroke, 14 (64%) were previous drivers, 5 (23%) drove to the clinic and 4 (18%) recalled previous driving advice; none of these 4 patients had driven to the clinic.

Doctors referring patients to TIA clinics need to recognise their medicolegal obligation to inform patients of the DVLA driving restriction.

076 MAGNETIC RESONANCE PERFUSION DIFFUSION MISMATCH IN ACUTE ISCHAEMIC STROKE: SYSTEMATIC REVIEW OF METHODS USED, INFLUENCE ON PROGNOSIS AND IMPACT ON RESPONSE TO THROMBOLYTIC THERAPY

I. Kane, P. Sandercock, J. Wardlaw. *University of Edinburgh, Edinburgh, UK*

Background: Acute ischaemic stroke patients with evidence of ''mismatch'' between perfusion and diffusion lesions on magnetic resonance may derive greater benefit from thrombolysis.
Methods: Systematic review of published reports of magnetic resonance PWI/DWI in acute ischaemic stroke to test this hypothesis. Data extracted: definition of mismatch, clinical and/or radiological outcome at one month, treatment with thrombolysis.
Results: Eleven papers met study inclusion criteria. There were five different mismatch definitions and at least 7seven different PWI methods amongst the 11 papers. Only three had useable data on mismatch, outcome and influence of thrombolysis (61 patients with and 18 without mismatch). In patients not thrombolysed, mismatch was associated with a non-significant two-fold increase in the odds of infarct expansion (OR 2.2, 95% CI 0.34 to 14.1), but this was similar in those thrombolysed (OR 2.0, 95% CI 0.37 to 10.9). Half the patients without mismatch had infarct growth. No data on functional outcome were extractable.
Conclusions: (1) Data are inadequate to use mismatch to select patients for thrombolysis. (2) The absence of mismatch does not mean that there is no ''tissue at risk''. (3) Patients without mismatch should not be excluded from trials of thrombolysis. (4) Standardised definitions of mismatch and perfusion are required.

077 MANAGEMENT OF HYPERTENSION AS A SECONDARY PREVENTION IN STROKE PATIENTS

A. Neligan, R. Renganathan, J. Spencer, B. J. Sweeney. *Department of Neurology, Cork University Hospital, Ireland*

Introduction: Control of hypertension is probably the single most effective intervention in secondary prevention after stroke.
Methods: In this retrospective study we examined blood pressure management on discharge in stroke survivors over a 6-month period.
Results: 137 patients were identified and of these 43.8% were male, with an age range of 22 to 94 years (average 71 years). Admitting speciality was noted. Risk factors for stroke, heart rate and blood pressure on admission were noted. 65% had previous hypertension, 41.6% had a previous TIA/CVA and 38% atrial fibrillation (32.3% new). 63.5% were on anti-hypertensives. Average systolic blood pressure (SBP) on admission was156 and diastolic blood pressure (DBP) was 83.

31.4% were started on anti-hypertensives at an average systolic blood pressure of 165 and 91 diastolic. While females had a poorer outcome, no clear gender differences in management were identified.

Overall blood pressure control was reasonable (average SBP 129, DBP 71); however, 68% had a SBP greater then 120 and 29.2% greater then 140. Only 3.6% had a DBP greater then 90 on discharge.
Conclusion: A significant percentage of stroke survivors were discharged with suboptimal blood pressure levels despite clear guidelines on stroke from the RCP.

078 THE AVAILABILITY OF CT AND MAGNETIC RESONANCE FOR ASSESSING PATIENTS WITH ACUTE STROKE IN THE UK

I. Kane, J. Wardlaw, P. Sandercock. *Division of Clinical Neurosciences, University of Edinburgh, Edinburgh, Scotland*

Introduction: Several experts recommend magnetic resonance scanning as the imaging method of choice for patients with acute stroke, especially for selecting patients for thrombolysis. We assessed the feasibility of magnetic resonance scanners as the primary imaging method in acute stroke.
Methods: Survey of all acute hospitals in the UK on availability of CT and magnetic resonance imaging. For centres with magnetic resonance scanners, we assessed magnetic resonance capacity to scan patients with acute stroke during (and out of) working hours (with an estimate of the number scanned in the last 6 months).
Results: Of the 268 hospitals, 248 (93%) responded of whom, 97% had a CT scanner and 78% had an magnetic resonance scanner on site. Of those with magnetic resonance scanners, access for patients with acute stroke was rated as at least ''difficult'' for 73% during working hours and for 95% out of hours. We calculated that, in the whole UK, each year, about 150 patients with acute stroke are scanned with magnetic resonance within 6 hours of symptom onset.
Conclusions: CT scanning is almost universally available and must remain the primary imaging method for patients with acute stroke. If new emergency treatments for stroke depend on rapid access to magnetic resonance imaging, further investment in radiology staff and equipment will be needed.